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THIRD SERIES FOUNDED BY EDWARD JACKSON

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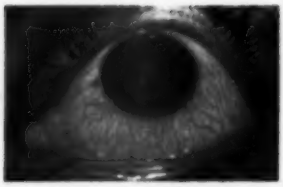

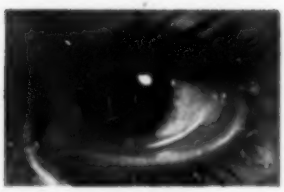

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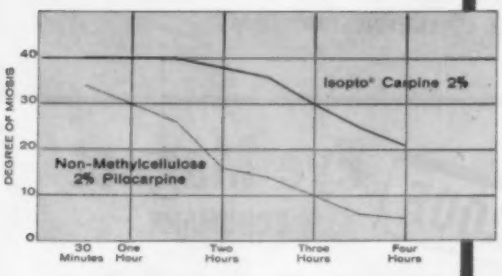

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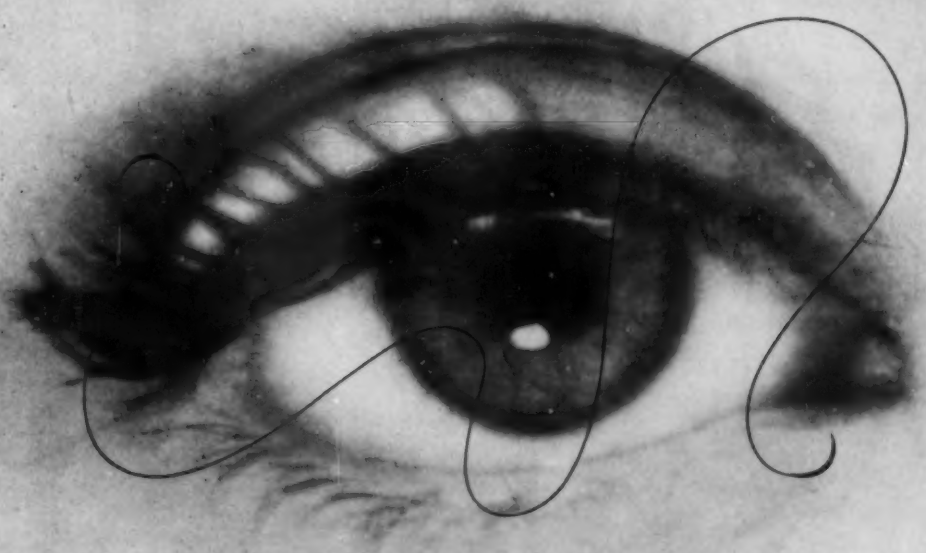

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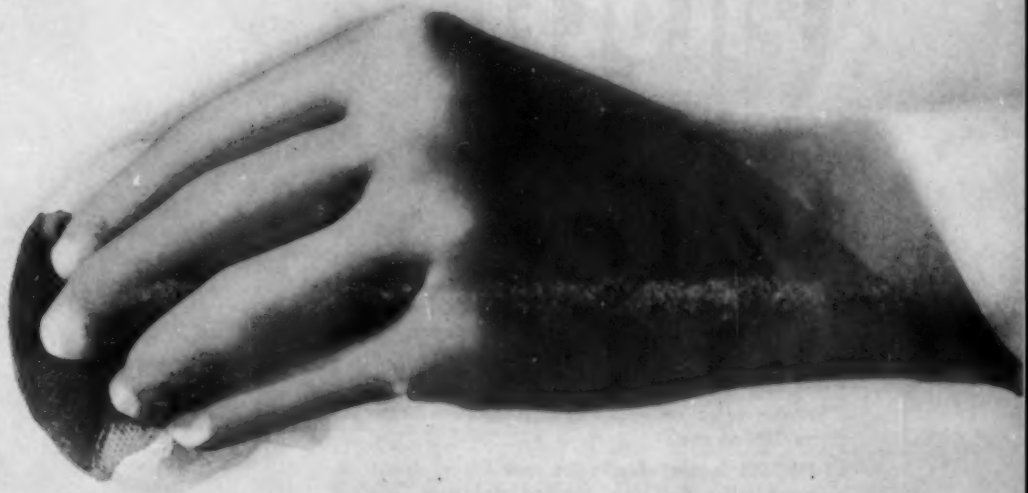

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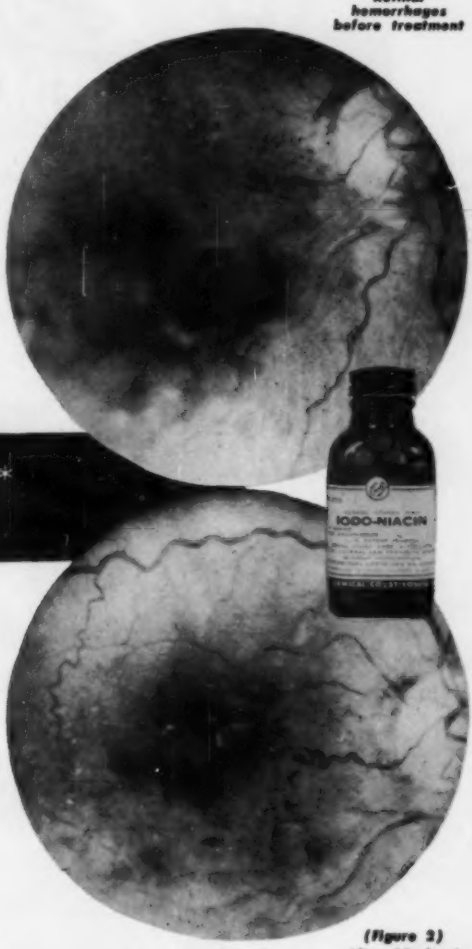
(Figure 1)
Retinal hemorrhages before treatment



(Figure 2)
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1. *Am. J. Ophth.* 42:771, 1956.
2. *Am. J. Digest. Dis.* 22:5, 1955.
3. *Med. Times* 84:741, 1956.

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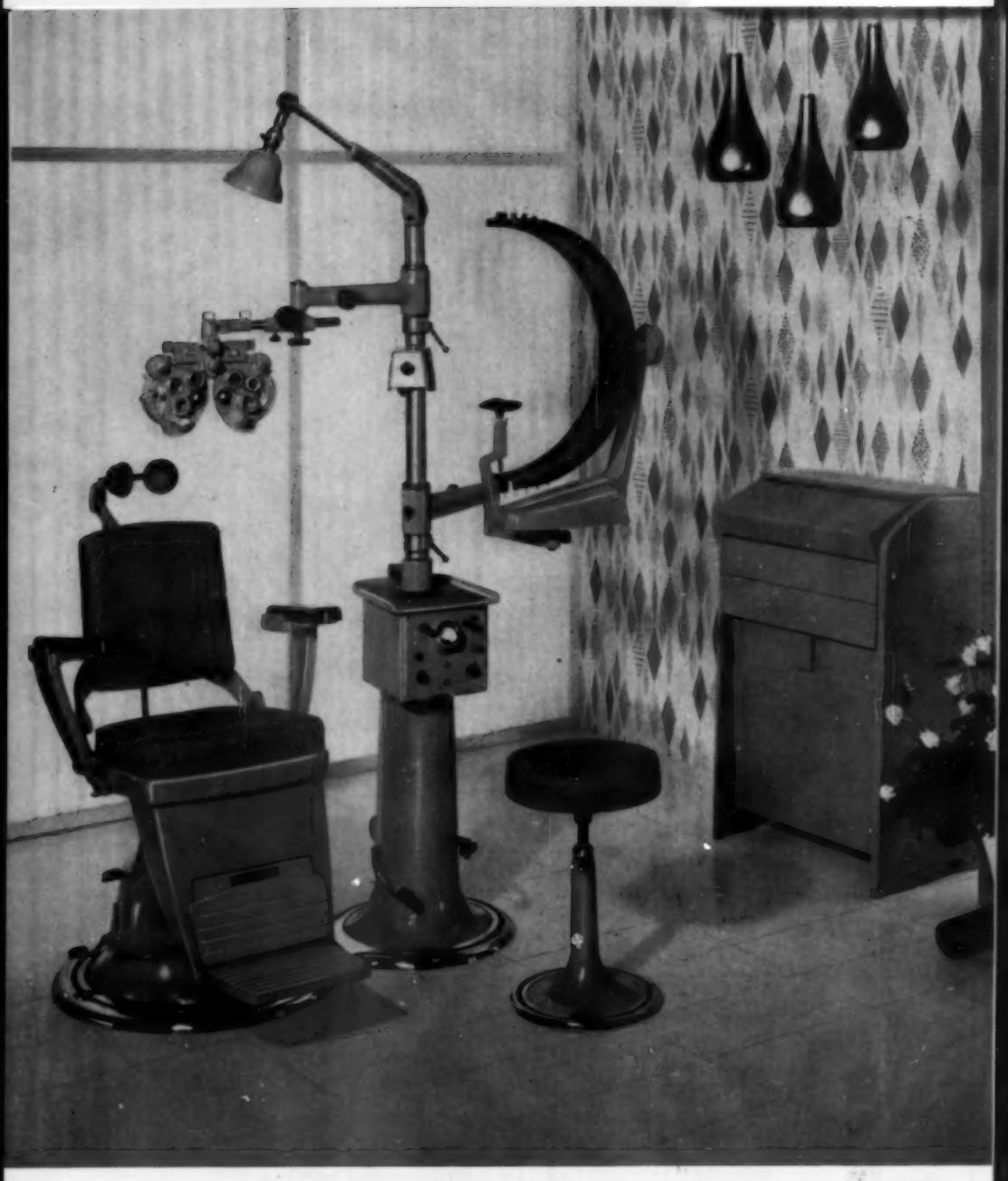

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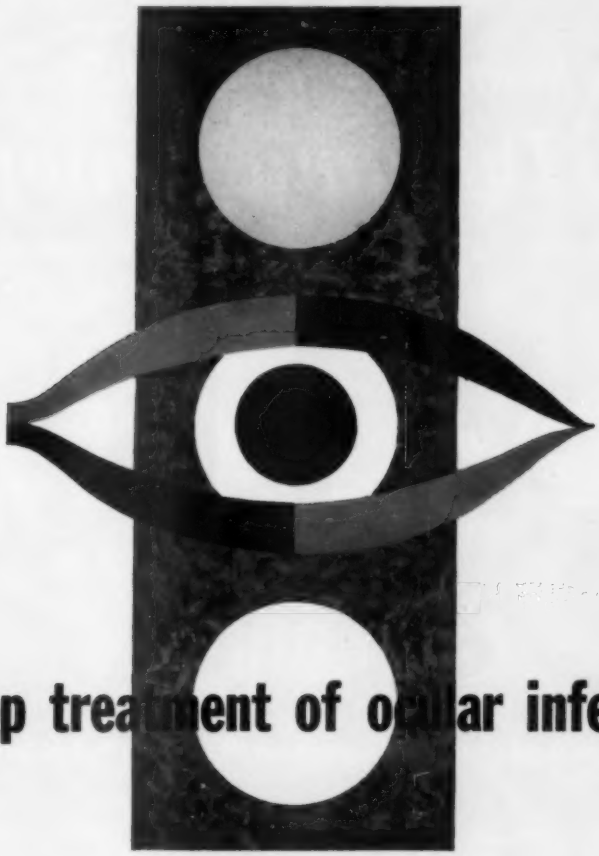

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Correct base curves are also very important because they can change the size of the retinal images. The size of the retinal image depends on the correction, of course, but also on the distance from the nodal or principal point of the eye to the nodal point of the lens. In a plus lens as this distance increases the image size becomes larger and in a minus lens the image size becomes smaller.

The position of the nodal point of any ophthalmic lens depends upon its curvature. It is upon this fact that the lenses to correct unequal retinal images are based.

The above facts are presented because they have a bearing on the case of Mr. S. which we present now. Mr. S. required a +1.50 sphere in each eye combined with a small cylinder. The correction had been worn comfortably for years. One lens was broken and replaced and Mr. S. immediately started having eye trouble.

He reported back to his ophthalmologist who checked the new lens for power, axis, position of the optical centers, etc., and found everything as it should be. The ophthalmologist then checked the base curve of the new lens and found it very different from the curve of the old lens. A new lens was ordered with the same base curve as the old lens and the patient's symptoms disappeared.

We think this case interesting because with unmatched base curves, the patient reported the most common symptoms of ocular image asymmetry: inability to read or do close work comfortably, discomfort at movies and headaches.

The amount of ocular image asymmetry induced in this case was small—less than one per cent. But very important because it resulted in unwearable glasses.

So many cases of this type have come to our attention that we present this one with the hope that it may not only solve an immediate problem but will also result in more control by the ophthalmologist of his patients' lens replacements.

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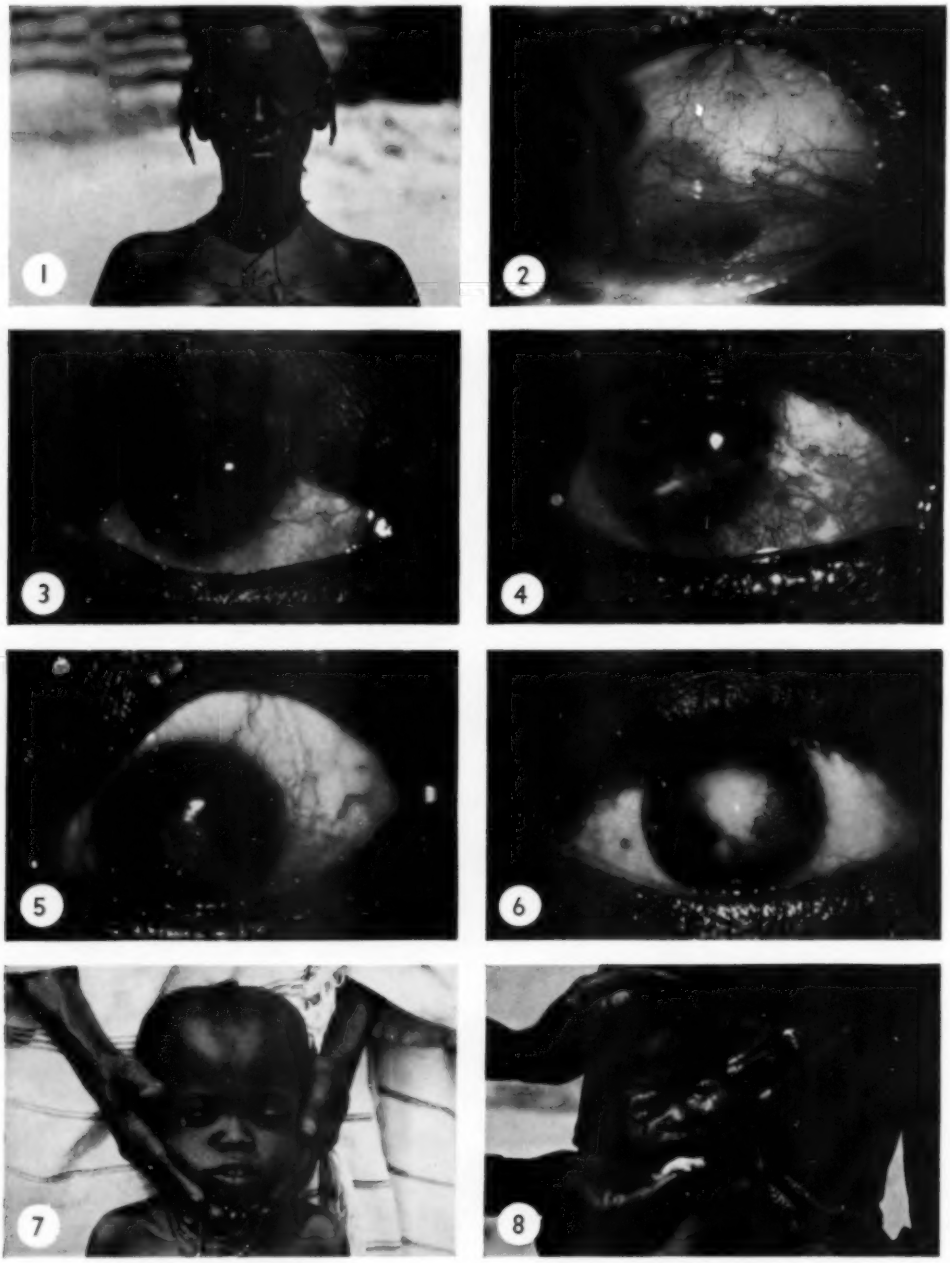


Figs. 1 to 8 (Rodger). Eye diseases in the African continent.
(1) Fulani girl whose left eye has been blinded by a thorn.
(2) Healed phlyctenulosis.
(3) Leproma of the outer canthus with early plastic leprous keratitis.
(4) The end-result of measles in Africa.
(5) Trachoma with pannus, central opacification due to trichiasis; pigmented apron below.
(6) Onchocercal sclerosing keratitis. The eye showed microfilariae in the pannus onchocercosus at biopsy.
(7) Congenital hydrocephalus and buphthalmos.
(8) Bilateral retinoblastoma.

AMERICAN JOURNAL OF OPHTHALMOLOGY

VOLUME 45 MARCH, 1958 NUMBER 3

EYE DISEASES IN THE AFRICAN CONTINENT*

F. C. RODGER, M.D.
Aligarh, India

The areas surveyed included the northern territories of Ghana, North Nigeria, and the highlands of the Cameroons. In addition, long treks were made into French Haute Volta, Niger, Sudan, and the Cameroons. The team travelled from Takoradi in the south to Timbuctoo, and via Lake Chad to the coastline at Lagos. In all, some 100,000 miles by lorry, jeep, horse, barge, canoe, or on foot were covered. The survey commenced in November, 1952, and finished in June, 1956; during this entire period, apart from two periods of leave, the team was actively engaged in ascertaining the causes and incidence of blindness. Six hundred days were spent in the bush living among the natives, the rest of the time being divided between certain large towns and, during the rains, in a clinic at each of our bases. In all, 5,716 cases were examined. The ocular biomicroscope in conjunction with the ophthalmoscope were the two instruments which proved of greatest importance. All the accessories to be found in a modern clinic were available. Illiterate African pagans, however, do not co-operate well with the examiner in such investigations as scotometry and gonioscopy. Subjective tests were always doubtful. As a result, it was extremely difficult at times to make a diagnosis.

The team had a pathologic unit which investigated conjunctival smears, blood films, gland punctures, urine, skin and conjunctival biopsies, and so forth. When further pathologic examinations not possible in the African bush were required, an attempt was made, not always a successful one, to take the patients back to the base where such procedures as X-ray studies of the orbit and serologic tests could be done at leisure. In other cases, particularly when investigating the posterior segmental lesion of onchocerciasis, specimens of serum were rushed to the airfield and dispatched in ice to the United Kingdom.

A feature of the survey was the number of important eyeballs which were obtained for subsequent pathologic examination. Twenty eyes, most of rare conditions, were sent to England, as well as 80 pieces of tissue. A photographic library of tropical eye diseases was compiled, and a special attempt made to assess the part nutrition plays in eye diseases among primitive people. To this end, specimens of food were sent to the United Kingdom for assay, and the dietaries of the different tribes recorded; special examinations, such as the use of a dark adaptometer, were also carried out. With the aid of these procedures, it is felt that the picture taken back on completion of the task was a fairly accurate one.

In addition to ascertainment of the facts, the main effort of the team was directed toward a fuller understanding of the clinical manifestations and pathogenesis of ocular onchocerciasis. To this end, resort was made to experimentation both with human and animal material. Such experiments were not unnaturally carried out in the field only with great difficulty, yet very often that was the only place they could be carried out.

It cannot be said that we answered all the

* This study was sponsored by the Commonwealth Society for the Blind and was made while Dr. Rodger was director of the British West African Ophthalmic Survey. He is now Research Professor of Ophthalmology, Muslim University.

questions we ourselves posed in relation to this interesting disease but we did answer some, and the very fact that we posed several new ones is in itself valuable. A great advance was made when a technique was evolved whereby the microfilariae of Onchocera volvulus could be isolated and kept alive for up to 24 hours in the laboratory. By this means, we were the first to be able to reproduce some of the manifestations of ocular onchocerciasis in experimental animals, and to study the course they took.

I. Incidence of blindness in West Africa

The incidence of blindness in the territories surveyed was extremely high; in the case of the northern territories of Ghana as high as 3,000 per 100,000. This must be about the highest incidence of blindness in the world, and is mainly due to the ravages of onchocerciasis. A general picture of the incidence of blindness in Africa has emerged, which is supported by figures from other parts of the world. In Europe, the incidence of blindness is about 200 per 100,000. Where trachoma exists the rate rises to about 500 per 100,000 or higher; in heavily endemic onchocerciasis areas the figure rises to over 1,500 per 100,000.

Remarkable as this last figure is, it is after all an average figure over a wide area of endemicity within which there is a gradation in the degree of the density of the infection; as a result in some areas the figure is higher still. In one village we visited we found 18 percent of the inhabitants blinded by onchocerciasis, and a local figure of 10 percent is not unusual in Northern Ghana.

Incredible though these figures are, statistics published by the Commonwealth Society for the Blind this year (in most cases agreed before publication with the governments concerned) support them. This report shows that in 39 Commonwealth or Mandate territories there are at least 650,000 blind people. The four West African territories, Nigeria, Ghana, the Cameroons, and the Gambia with 400,000 blind—about 1,000 per 100,000—constitute by far the largest group; the figures also show 152,000 blind in East Africa, 44,000 in Central Africa, 10,000 in the West Indies, and 25,000 in certain territories of South East Asia. The entire population covered by these territories is 79 million, so that our own figure of 3,000 blind per 100,000 for Northern Ghana, although high, is by no means inconsistent with the over-all picture.

II. Standard of blindness used

There has always been some discrepancy in the standards of blindness used by workers among primitive peoples. This is largely determined by practical considerations. The American standard of 20/200, that is the equivalent of 6/60 Snellen, was accepted by the Expert Committee on Onchocerciasis of the World Health Organization in 1953, but at a second conference in Leopoldville in 1954 there was some disagreement about this. A body of opinion favored a less rigorous standard, namely 3/60 Snellen. There is little to be lost in Africa, where most of the people are agricultural laborers, by adopting a less rigorous standard. Trousseau's standard of "inability to count fingers at one meter," that is 1/60 Snellen, is theoretically even more attuned to reality.

In the absence of an agreed standard, we used the latter to classify our cases as blind, but, in addition, recorded as part-blind all who could count fingers at one meter but were unable to see 6/60 Snellen. To our surprise, within the margin on the two groups there was remarkably little difference when we came to assess them at the end of the survey, so it would seem that it does not matter very much which of the recognized standards is adopted. Our efforts might be better directed to standardizing the size of the fingers counted, and the conditions under which they are counted!

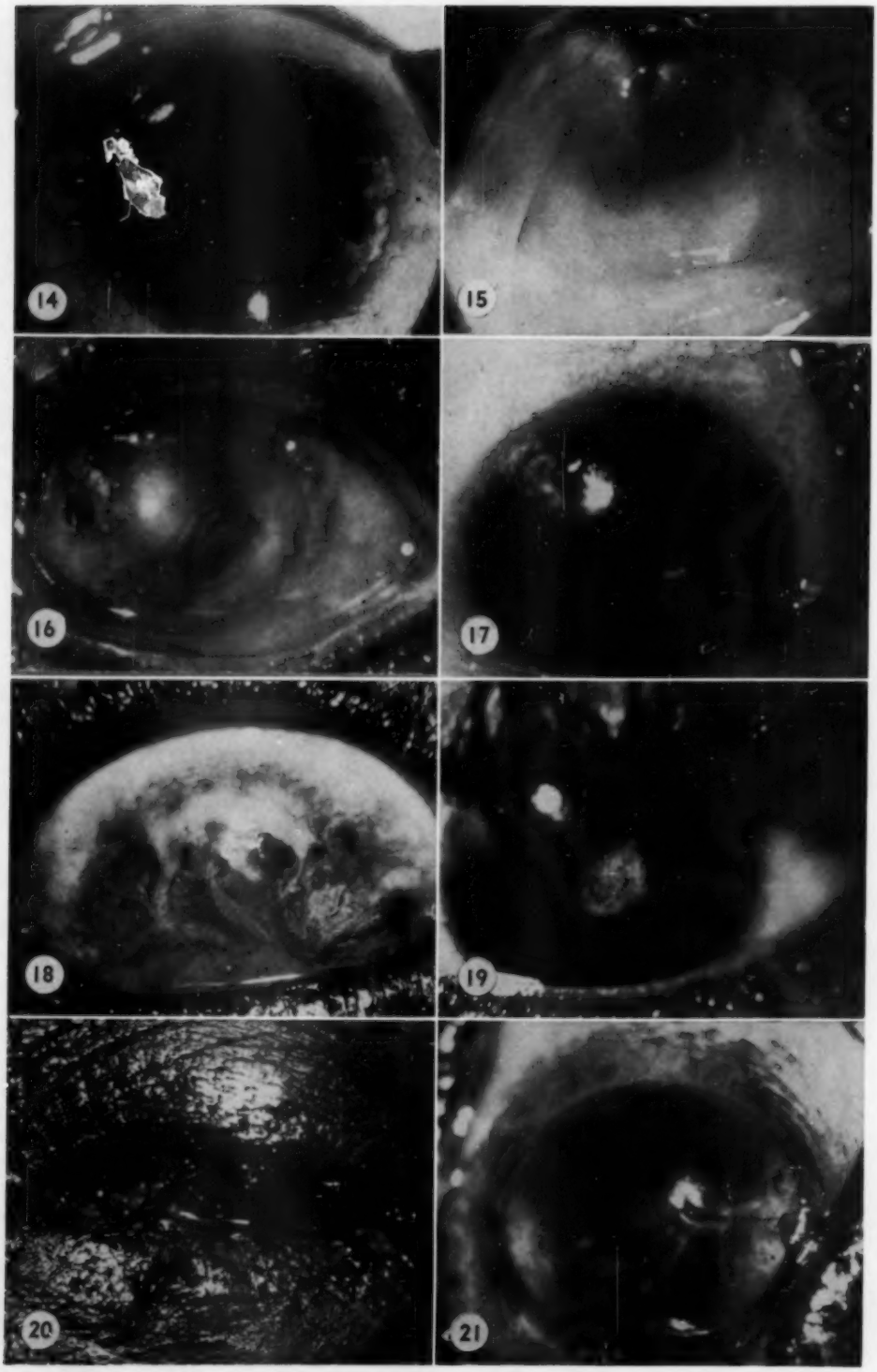
III. Congenital ocular anomalies

Remnants of the pupillary membrane are fairly commonly observed with the slitlamp in the African eye. In the fundus, Berg-

Figs. 9 to 13 (Rodger). The survey team at work. (9) Examining Hausa patient in North Nigeria. (10) Selection of suitable patients. The clinic is under canvas here, and the tents are pitched in the mountains of the Plateau Province of North Nigeria. (11) The pathologic technicians are examining skin biopsies and thick blood films on the balcony of a bungalow during the rains. (12) A skin biopsy being taken from the neck. In the good weather the technicians worked outside. (13) During the rains we returned to base and carried out clinical experiments. Here the filaricidal action of a drug is being investigated. The drug is being administered by intravenous transfusion because of its toxicity.

meister's papilla, congenital veils, and persistent hyaloid arteries were seen on several occasions. Congenital cataracts are not common, only a few cases being recorded.

A common and unusual finding was that of atavistic pupillary fringes. Eccentric pupils were recorded in a few instances. One or two aneurysms of the retinal arteries were noted in the course of the survey, and macular degeneration was seen in three children, being presumed to be of congenital type. Nystagmus was recorded only twice, in children, and the probability is that it was due to congenital syphilis. Buphthalmos in association with a congenital hydrocephalus was seen as a rarity, and only a few cases of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high myopia occurred. Ptosis of congenital origin was also extremely rare.

Congenital ocular defects following intrauterine infections were not nearly as common as in Europe; ocular syphilis, usually evincing itself as an interstitial keratitis, was a fairly common lesion, and there were several cases of pepper-and-salt fundus. No cases of ocular defect following virus infections in pregnancy were noted.

We have on record two cases that clinically closely resembled an old punched-out depressed toxoplasmic chorioretinitis. We were unable, however, to confirm the diagnosis.

IV. Senile anomalies

Senile cataract is one of the most common causes of blindness in this part of the world. It is usually cortical in type but may reveal itself as a nuclear sclerosis. Atrophy of the iris stroma and pupillary fringe is very common indeed, as is the presence of pigment particles over the lens capsule. Central macular degeneration appears in about the same proportion, it would seem, as it does in Europe. Senile choroidal sclerosis, on the other hand, is more common than in temperate climates. Arcus senilis is not as common as in Europe.

V. Dystrophies and degenerations

In the cornea, especially in association with keratitis, calcification, several varieties of lipid degeneration, and epithelial bullae are extremely frequent. The condition known as band-shaped opacity of the cornea is remarkably common. It may be seen alone, or in conjunction with an anterior uveitis. Within the eye colloidal degeneration of the retina and Tay's choroiditis cropped up occasionally. Asteroid bodies and synchysis scintillans were observed several times.

A condition we have called arcus tropicalis was seen in all age groups; this condition is not a variety of arcus senilis; it differs from it in a few important respects: the opacification is superficial only; there is no clear zone between it and the limbus; and it is always complete. Pathologically it consists of invasion close below Bowman's membrane by chronic inflammatory cells with a few fibroblasts. We believe it is climatic in origin.

VI. Nutritional anomalies

In the territories covered, there was a widespread low-grade deficiency in vitamin A. No members of the B-complex were on short supply, except riboflavin, the intake being only three quarters of normal. At the southern margin of our survey area, however, where the high forest began to appear, vitamin A was seen in plenty. An opportunity was thereby afforded of comparing cases in "vitamin-A-deficient" regions with those in "vitamin-A-full" regions. Bitôt's spots were seen surprisingly enough in their classical form on only a few occasions; more commonly a prexerotic stage was seen where, in the classic situation of a Bitôt spot, there appeared a small whipped-up patch of clear mucus. This we saw especially in people suffering from night blindness, and with a suspicion of the dermatosis of vitamin-A deficiency, so that we were forced to conclude that it was the pre-Bitôt sign of vitamin-A deficiency.

Xerosis corneae on the other hand was extremely common, especially where in addition to the vitamin-A deficiency there was a defect in corneal diffusion due to a concomitant ocular lesion. It is reversible in some

←

Figs. 14 to 21 (Rodger). Some eye diseases in the African continent. (14) Band-shaped opacity of the cornea. (15) Advanced stage of hyperplastic leprous keratitis. (16) Advanced stage of keratomalacia. (17) Mutton-fat keratic precipitates in tuberculous anterior uveitis. (18) The result of native medicine. (19) Pigmented fibrous membrane occluding the pupil in a cerebrospinal meningitis anterior uveitis. (20) Trichiasis and entropion with secondary infection in trachoma. (21) Marked vitamin-A deficiency, with rucking and pigmentation of the bulbar conjunctiva and xerosis cornea.

instances. Brown pigmentation and slack folds of the lower bulbar conjunctiva were seen a lot in vitamin-A deficient regions, and we rather tend to agree with those workers who state that this is a sign of avitaminosis A. Night blindness was a frequent complaint, especially in children.

Keratomalacia was a difficult condition to diagnose, but it appeared to be part of the picture wherever a chronic keratitis supervened. The classic type of keratitis of which we are thinking is a phlyctenular one; here in the adjacent areas of the cornea there was plentiful evidence that keratomalacia exists in Africa. The seven types of obscure malnutritional keratitis described by Blumenthal (1950) may all be explained on this basis. Spontaneous clean iris prolapse is the common end-result of keratomalacia in small children. On cauterizing such prolapses with trichloracetic acid and bolstering the vitamin-A intake the condition rapidly improves. It is interesting to note that any one of these signs of avitaminosis A might occur by itself, and with the exception of hemeralopia might be unilateral.

Optic neuritis following deficiency of the B-complex—my own view being that a mixture of thiamin and riboflavin deficiency, especially the former, is the cause (Rodger, 1953, 1954)—was very rare, and the defect of vision was always associated with a local famine. There is no doubt that the thiamin intake of the peoples among whom we worked was adequate, and although the riboflavin intake was below the international requirement (75 percent), it has never been my view that riboflavin deficiency in itself leads to an optic atrophy. My experiences in Africa lend support to this view.

Finally, there is the very interesting posterior lesion, often associated with only a minor infestation by Onchocerca volvulus, the chorioretinopathy of onchocerciasis. This condition was found only in areas where the vitamin-A intake was poor in the dietaries. We carried out a lot of experimental work on this, and improved the condition greatly by administering massive doses of Crook's cod-liver oil capsules. The subject, however, is a complex one, and has been written up in full elsewhere (Rodger, 1957).

VII. Diseases of the lids and orbit

The most common lesion in this area was an orbital cellulitis. Orbital tumors were also very frequent, especially hemangiomas. Dacryocystitis was extremely rare; only once was an onchocercoma of the lid seen; chalazia were not observed except in visitors to the region. A periorbital "contact allergy" dermatitis was recorded on several occasions, usually in association with, and as a result of, a secondarily infected trachoma.

VIII. Conjunctival diseases

By far the most important conjunctival disease was trachoma. As distinct from the corneal pannus, which was characteristic, infection of the conjunctiva was for the most part papillary rather than follicular in nature; this perhaps explains why for so long it was thought that trachoma did not exist in West Africa. We noted that in children a fulminating type of trachoma, leading to complete opacification of the cornea within a year, was extremely common; we have not seen this type described anywhere else. The clinical picture was a classic one inasmuch as it was in the fulminating type almost alone that trachoma follicles were observed; it was invariably accompanied by a great migration of melanophores into the palpebral conjunctiva, the final appearance being rather like acanthosis. We called this trachoma nigricans.

Purulent conjunctivitides due to the Koch-Week's bacillus, or to the pneumococcus, and frequently going on to corneal ulceration in their neglected state, were seen in many villages. An irritant catarrhal type of conjunctivitis was seen, unassociated with any specific organism, and discovered to be due to the widespread practice by men, women, and children of using antimony around the roots of the lashes as an adornment; some

of the metal entering the lower fornix gives rise to it.

The limbitis of spring catarrh occurs fairly frequently, especially in the young. Corneal involvement was rare. It responds readily to steroid therapy. The adenoidal follicular conjunctivitis of adolescence is common. An angular conjunctivitis due to the Morax-Axenfeld bacillus appeared every now and then, and a conjunctivitis that may well prove to be purely irritant due to the dust-filled air was found in those regions skirting the desert.

Despite rumors to the contrary, we did not find invasion of the conjunctiva (or of the cornea) by the gonococcus. Only one proved case of ophthalmia neonatorum of this nature was found, most of the purulent blenorrheas of infants proving to be inclusion virus blenorrheas. We saw several cases of lipoma and leproma of the conjunctiva.

A membranous conjunctivitis—simulating the self-inflicted "sepoy" conjunctivitis seen by me in India—was extremely common, in most instances being due to native medicines. The classic site of this condition is in the lower fornix involving the lower half of the globe. One drug that is particularly dear to the African, being on sale at every little market, is mentholatum, and we saw several cases where this irritant unguent had been inserted in the lower fornix of a previously slightly affected eye; the result was usually a disastrous corneal opacification.

Nevi of the conjunctiva were seen frequently, and in two instances they revealed malignant changes; one case of precancerous melanosis was observed; on the whole malignant tumors in this tissue were rare.

By far the most common tumor of the conjunctiva is the pinguecula. We believed for a while, after comparing the records in vitamin-A deficient zones with those in the high forest where vitamin A is plentiful, that in the latter these small benign tumors are not nearly so frequent; we felt it might be that an avitaminosis A played a part in its pathogenesis. Now we are not so sure. We were particularly interested in the relationship of a pinguecula (and early pterygium) to onchocerciasis, the first evidence that onchocerciasis has invaded the cornea being frequently at such a site. It would appear that the pathogenesis of the pannus onchocercosus depends upon the invasion of the cornea and the subsequent death of the microfilariae, and therefore it might be that the parasites find it easier to penetrate the limbal cul-de-sac from the subconjunctival space when such a tumor exists.

Fatty excrescences were seen in the palpebral conjunctiva of the upper lid and frequently preceded calcareous deposits in that region.

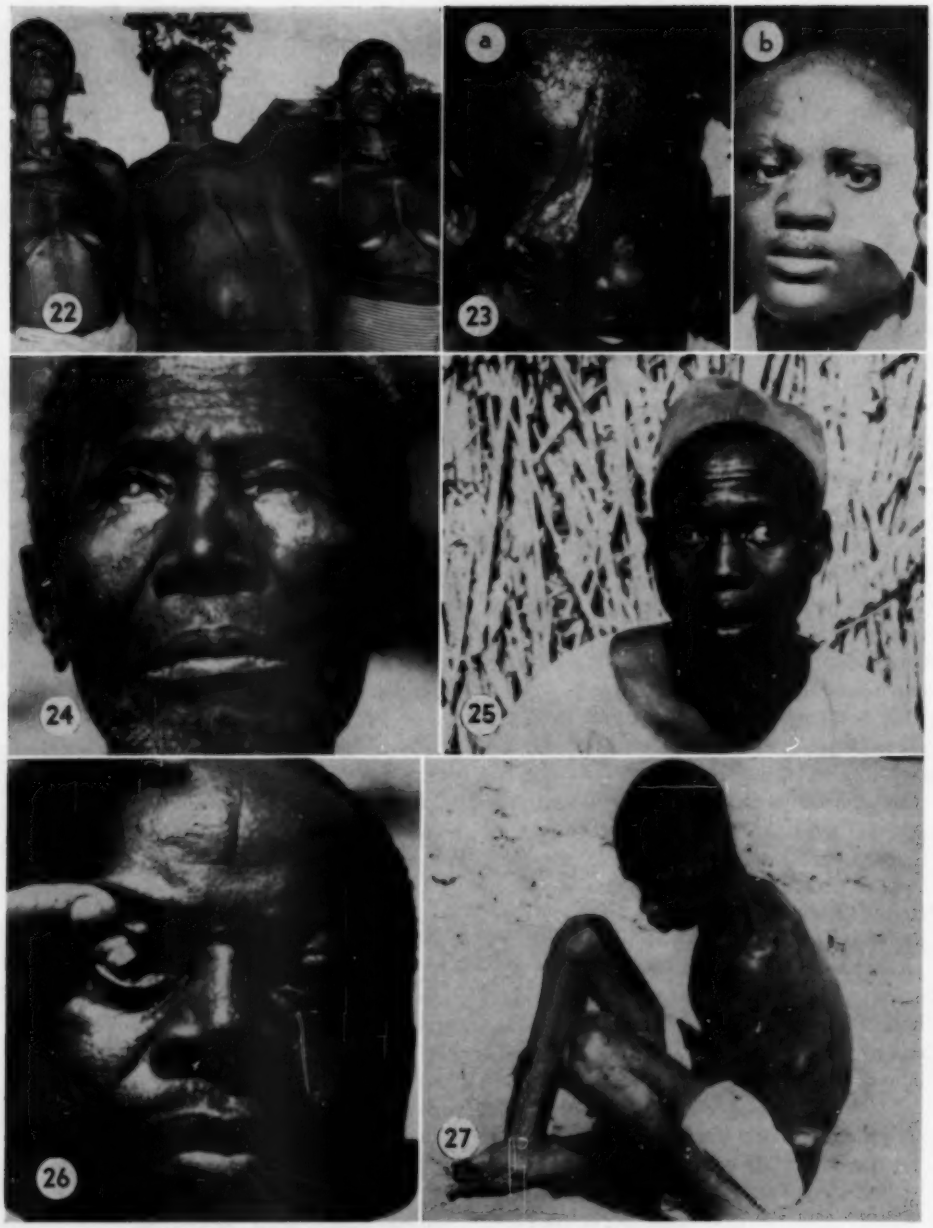
IX. Corneal diseases

In endemic onchocerciasis areas there is no question at all that an onchocercal keratitis is by far and away the most common finding. This keratitis is typically due to the invasion of the cornea by pannus which forms round the dead bodies of parasites which have invaded the cornea and died there. In addition, there may be in relation to the tongue of the pannus a few superficial or deep punctate corneal opacities. These opacities are invariably dense in color and may become confluent, thereby adding to the size of the pannus.

The condition usually starts either at the 3- or 9-o'clock positions and characteristically occupies the lower half of the cornea, in this way being readily distinguished from pannus trachomatosus. The lesion is a sclerosing keratitis. In addition, inflammation at the limbus can occur, and the term limbitis seems to be a good one, for the condition often becomes quiescent at that stage, not going on to a true keratitis.

Of equal importance in Africa, although not nearly so frequently seen in endemic onchocerciasis areas, is pannus trachomatosus, whose characteristic appearance is well known.

The next most common corneal condition is punctate keratitis; in addition to that due



Figs. 22 to 33 (Rodger). Types of patients encountered in course of survey.

(22) Three Sissala women with one eye between them! Each suffers from ocular onchocerciasis (River Blindness). North Ghana.

(23) A Bana tribesman seen in the southern Cameroons. A cutless wound involving the orbit, with

to onchocerciasis, the Herpes febrilis variety and that of the epidemic virus are very prevalent.

Epidemic keratoconjunctivitis has not previously been reported from this part of Africa but there is no doubt it occurs. In institutions outside the endemic onchocerciasis areas many such cases were seen. For example, of 120 boys seen in a training college, 31 of them suffered from it.

Tuberculosis of the cornea has always to be kept in mind, the most characteristic manifestation being a phlyctenulosis. However, an interstitial keratitis and a sclerosing keratitis due to this disease were also seen and are difficult to distinguish from onchocerciasis. The interstitial keratitis of syphilis was seen a great deal also, more often in acquired syphilis than in congenital, it seems.

Purulent keratitis, either simple ulcers due to abrasions, or serpiginous ulcers, or corneal ulceration in the specific fevers, constitutes a large part of ophthalmic practice, especially the latter. One of the main causes of blindness in Africa is undoubtedly corneal ulceration, often associated with rupture and inclusion of the iris following smallpox, measles, and even chickenpox.

In leprosy, an infiltrative lepromatous superficial or interstitial keratitis and a sclerokeratitis were observed. Of the tumors, two cases of the rather rare Bowen's disease were recorded. A postherpetic disciform keratitis cropped up every now and again, but it is interesting to note that only one case of typical dendritic ulcer was seen; the usual manifestation in Africa of Herpes corneae is a punctate keratitis.

Degenerations and dystrophies have already been described. They were frequently associated with poor nutrition or with concomitant uveal disease.

Band-shaped opacities appeared in nearly every village visited, and chalky deposits, epithelial cysts, lipid degenerations (often crystalline in type), and bullae in association with various types of keratitis and anterior uveitis were a commonplace.

Bedewing of the epithelium in glaucoma was only rarely observed; this disease will be discussed later separately. Rucking of Descemet's membrane, especially in conjunction with syphilitic interstitial keratitis, was noted quite frequently. Xerosis corneae, as has been mentioned already, was a frequent complication in diseased eyes in vitamin-A deficient areas.

Traumatic lesions were a frequent cause of leukomas. They were frequently due to penetration of the cornea by thorns or branches while the subjects were walking in the bush. Scarring of the cornea due to the application of native medicines has been mentioned already; gun-shot wounds of the eye cropped up every now and again, which is not surprising in view of the antiquity of the Dane guns used by the hunters.

Finally, one should mention the presence of ectasias in association with the sclerokeratides of leprosy and of tuberculosis, and the

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destruction of the eye. The patient walked 90 miles to attend the survey clinic, arriving three days after the injury. (a) Before treatment. (b) After treatment.

(24) An old man of the Tiv tribe blinded by trachoma. Hooding of the upper lids is characteristic. Benue River country, Nigeria.

(25) Optic atrophy associated with a divergent strabismus in a luetic basal meningitis is common. Hausa tribe, Nigeria.

(26) The use of market remedies and native medicines causes a certain amount of blindness. Here a Jatau tribesman applied menthol ointment to the lower fornix because of a purulent conjunctivitis. This caused total keratinization of the cornea and heavy pigmentation. North Nigeria.

(27) Trypanosomiasis and onchocerciasis. The patient has been blinded by the latter. Two onchocercomas can be seen on his left flank. He is a member of the remote Dakka Chamba tribe in the north Cameroons-Adamawa border. The survey team had to walk through dense bush for over 20 miles to reach this village.

vast number of cases in which anterior staphylomas or phthisis bulbi were observed, and for which no firm diagnosis was possible.

X. Disease of the iris and ciliary body

Once again it must be said that in endemic onchocerciasis areas, the most usual lesion of the anterior uvea was due to that disease. In fact, onchocercal anterior uveitis is the commonest disastrous complication of ocular onchocerciasis. It is frequently accompanied by invasion of the posterior uvea giving rise to an exudative uveitis. The pathogenesis of these conditions is the same as in the case of the cornea—a reaction around dead parasites. On several occasions we performed iris biopsies, and discovered the parasites wriggling in the stroma.

The clinical picture is similar to an anterior uveitis due to any foreign protein (for example, egg albumen). In onchocerciasis, however, it usually advances to complete occlusion of the pupil. It would appear that the pupillary margin of the iris is more frequently affected than anywhere else; this may be due to the fact that the parasites which invade this tissue (usually from the root) will in the end die at the inner ring whence they can go no further.

At any rate, whatever we may conjecture here, the clinical appearance of an onchocercal anterior uveitis is heralded by great exudation around the pupillary margin. If the condition settles, then the resultant exudate covering the pupil will shrink and break up, usually leaving some remnants at the pupil, and almost invariably causing complete depigmentation of the posterior pigment-epithelium fringe.

As the acute phase does not last very long, the condition was more frequently seen in its quiescent stage, and for that reason early workers described the iritis of onchocerciasis with its associated depigmented fringe as an insidious lesion (Hissette, 1937). This is only sometimes true.

Idiopathic nongranulomatous anterior uveitis appears to be as frequent a condition as it is in the clinics of the West; granulomatous states associated with flare, efflorescences, and mutton-fat keratic precipitates were found by us to be frequently associated with a serologic test positive for syphilis. Without doubt, many of these two lesions must also be due to tuberculosis, which has a fairly high incidence in the northern territories of the countries we visited.

Cerebrospinal meningitis, which in these territories has led to several devastating epidemics in the past, was usually evinced in the eye by the association of an anterior uveitis with deafness. The anterior uveitis was one in which the pupil was completely occluded, and in which characteristically the white membrane was covered with dense pigment. Such a massive migration of melanin in occlusion of the pupil was not seen with any other disease. In all cases where the anterior uveitis had been so severe as to occlude the pupil, there was degeneration of the suspensory ligament of the lens and secondary cataract. We frequently observed, either when the membrane had shrunk or had never formed, subluxation or dislocation of the lens for this reason.

In leprosy we saw more cases of lepromatous miliary iritis (that is with leprous "pearls") than we did the diffuse leprous type.

Sympathetic ophthalmia, which in a late stage is difficult to diagnose in an African, would appear to be a more common cause of blindness than it is usually given credit for.

Tumors of the iris and ciliary body are rare and were not seen except in one unusual instance: this was a case of neurofibromatosis, where the right iris was involved; the pupil consisted of a fibrous ring attached to the posterior surface of the cornea, and in the 9-o'clock sector there was a fibrous anterior synechia. In three cases a malignant melanoma fungating through the cornea was seen, in none of which the tissue of origin could be determined. They might better have been reported in the next section. This num-

ber of melanomas was present in our first 1,500 cases, and we can assume, therefore, that they are more than three times as frequent in Africa than they are in the United Kingdom.

XI. Choroidal diseases

Once again in heavily endemic onchocerciasis areas it was this disease which appeared to be responsible for the majority of the choroidal lesions seen. They are of two varieties: a posterior exudative chorioretinitis which is always associated with the anterior uveitis already described, and a degenerative chorioretinopathy with a complex etiology.

Apart from onchocerciasis a not inconsiderable number of cases of choroidal disease were seen, most of them being of syphilitic type outside of North Gold Coast. In addition, tuberculous exudative choroiditis was noted, either in the acute stage or presenting the highly suggestive picture in the later stages of a circumscribed lesion of the choroid around the posterior pole.

It may be that many of the disseminated choroiditis cases we considered to be luetic in origin were in fact tuberculous, but a very high proportion of them revealed serologic evidence of the former. As a retinitis is an almost invariable complication of choroidal inflammation, this subject will be gone into in greater detail in the next section.

XII. Retinal diseases

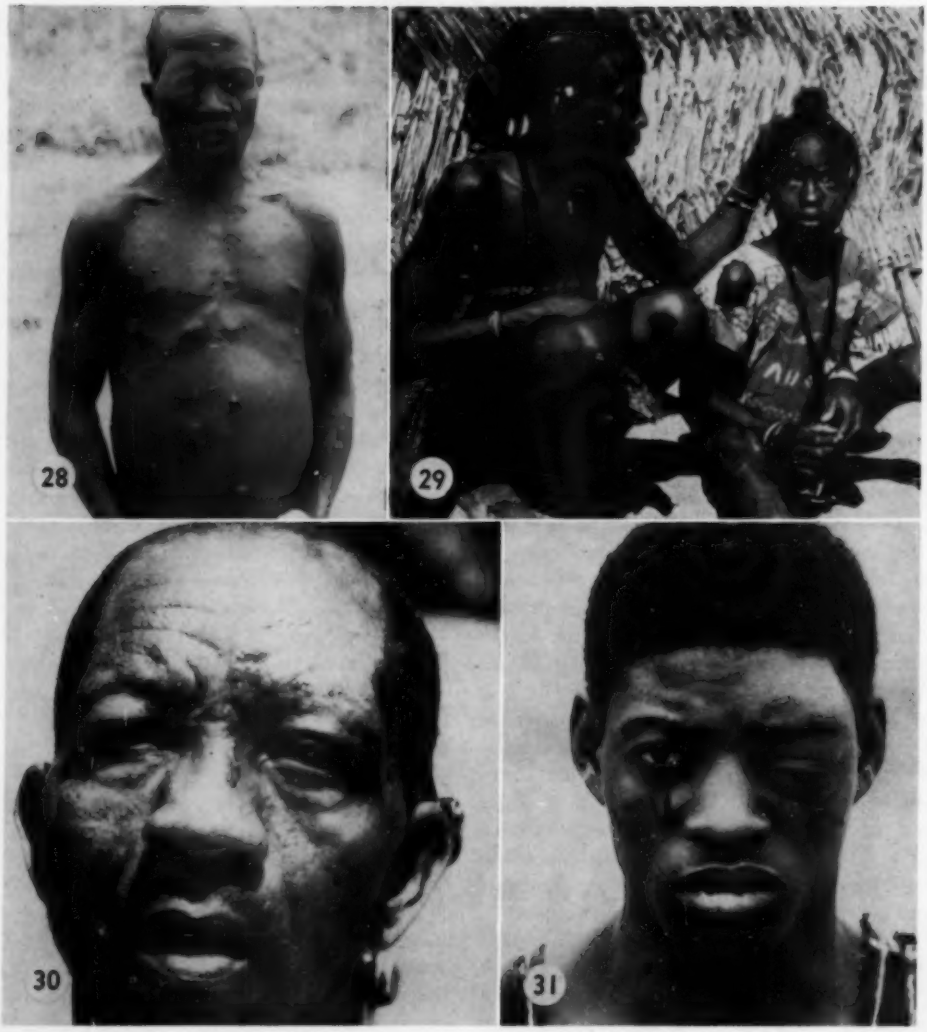
While the end-picture of the chorioretinopathy of onchocerciasis is remarkably similar to that of a choroidal sclerosis, the clinical history and appearances suggest that in the first instance the disease may well arise in the retina. Toulant and Boithias (1954) have published photoretinographs of this lesion. There is no doubt that it is remarkably difficult to distinguish between the chorioretinopathy of onchocerciasis and chorioretinitis due to syphilis or tuberculosis, especially when one has to make one's diagnosis in the bush. On clinical grounds alone there are times when one just cannot make a decision. The people we were working among found it difficult to answer even simple questions, so the history gave little help.

Colloid degeneration was seen not nearly as much as in Europe. Isolated pigment spots, usually one or two in number, large black masses of pigment, usually in the periphery, and a typical pepper-and-salt fundus appeared fairly regularly. One supposes there is no doubt that they are of luetic origin. Disseminated chorioretinitis, central exudative circumscribed chorioretinitis, and a neuroretinitis in association with a secondary retinitis pigmentosa were all frequently seen. Retinal vascular disease was seen in only one case, a hyperpiesia with retinal hemorrhages. The African does not appear to suffer from the usual retinopathies. One assumes that this may well be different in the more civilized coastal regions of Africa. One case of bilateral retinoblastoma in a child of two was seen, as were four cases of disciform degeneration of the macula.

XIII. Diseases of the optic nerve

While we never observed a proven case of ocular disease due to trypanosomiasis, we know that such conditions occur (Toulant, 1950). Nevertheless, sleeping sickness is still somewhat of a problem in the territories we covered. Tryparsamide being used freely in its treatment not so very long ago, there still appeared every now and again a case of tryparsamide optic atrophy with a very clear-cut history. One of the commonest types of optic atrophy which emerged was that associated with juxtapapillary chorioretinitis and a divergent strabismus. While the former might not be present, the latter was invariably so.

We were able to subject a number of these cases to serologic tests, and there seems no doubt that the cause is syphilis. In fact, we would go so far as to say that the association of an optic atrophy with a divergent strabis-



(28) Multiple neurofibromatosis with ocular involvement. A Hausa beggar.
(29) A Fulani mother with a 12-year-old child blinded by trachoma. Seen in Adamawa Province of North Nigeria.
(30) Herpes zoster in a Bamenda tribesman in the Cameroons.
(31) Orbital hemangioma in a youth of the Munchi tribe. Nigeria.

mus is characteristic. It is almost certainly caused by a basal meningitis in the secondary stage of the infection. We never saw Tabes dorsalis nor general paresis, nor an Argyll-Robertson pupil. In cases with a positive serologic test and a well-remembered history it was not difficult for us to categorize some of our cases as neurorecidive reactions or Jarisch-Herxheimer. Conditions predispose to interrupted treatments in Africa! Six cases of neuritis papulosa were also noted.

Cerebrospinal meningitis as a cause of optic atrophy was also observed, invariably without an accompanying anterior uveitis. The optic atrophy of glaucoma will be considered later.

There still remains an extraordinarily high number of cases of simple optic atrophy among people in whom Tabes dorsalis is not seen. Some of these tabeticlike atrophies might well have been manifestations of a genetically determined anomaly such as Leber's disease. As some cases of choroidoretinal degeneration of young people appeared in the same districts (the cause for which we also believe to be genetic) this might well prove to be true. Most tribal laws forbid inbreeding; nevertheless, in a few cases we broke through the reticence of our subjects who admitted in the end that there had been inbreeding in their family. This was particularly the case in the Cameroons, where the head men and chiefs have such a vast number of wives (without being at all facetious about it) they often lose trace of their children. Their wives remember such relationships, however, and if it suits them remain silent. The principal cause of most of these optic atrophies must, nevertheless, be something else.

As mentioned earlier, nutritional amblyopia is rare; similarly, onchocerciasis is not an important cause of optic atrophy, for the greatest number of simple optic atrophies that we recorded were in nonendemic areas. Trypanosomiasis as a cause is also geographically restricted. When, of course, the patient has a high microfilarial count in the conjunctival biopsies and an optic atrophy, then onchocerciasis as a cause must be considered; my private view is that it is unlikely to occur in the absence of an associated onchocercal ocular lesion.

With no other evidence as strong as that in favor of syphilis as a cause, we have classified all our simple optic atrophies of unknown origin as probably luetic. That may very well prove to be the correct classification after all.

XIV. Diseases of the lens

Senile cataract is one of the four most common causes of blindness in Africa. Congenital cataracts are extremely uncommon; traumatic and secondary cataracts are collectively almost half as common as the senile group. I have frequently seen in all types of cataract, subluxation and dislocation of the lens. It appears to be the natural course of events in onchocercal uveitis. One must not forget that "malams" still practice lens couching in every district of Africa.

XV. Diseases of the vitreous body

Both anterior bodies and synchesis scintillans were seen in several cases. Fluid vitreous was not as common as one might have expected. Twice we saw microfilariae in the vitreous body.

XVI. Tropical infections of the eye

Several conditions peculiar to the tropics have already been mentioned. Many cases of invasion of the eye with filariae loa were seen, but that never leads to ocular damage. We were constantly on the look-out in cases of orbital proptosis for cysticercosis and hydatid disease as a cause; they were never found. It has been mentioned already that although we examined many trypanosomiasis cases we never yet discovered in those who were blind that the cause had been that disease. In most of our cases the subjects had been blinded by onchocerciasis. This was also true of a great number of the lepers we examined, and it may well be that earlier workers were misled in this way. We observed not a few cases of yaws which had involved the orbit, and subsequently the eye. There were several instances of blindness which were said to have been due to a snake venom ophthalmia. We carried out conjunctival scrapings whenever there appeared to be a good reason for it. It was noted that in the vitamin-A deficient areas the xerosis bacillus was the most common inhabitant of the conjunctiva. One case of lymphogranuloma venereum was observed, revealed by

(32) An old Birom tribesman blinded by trachoma. North Nigeria.
(33) Female adult loa loa 64-mm. long removed from the eye of a Fanti nurse of the North Ghana.

the characteristic inclusion bodies, and clinically represented by a sclerokeratitis.

The young eye doctor coming to Africa usually arrives with his head full of metazoan and helminthic conditions, when, in fact, he would be better armed if he were to consider first the sorts of condition that appear in a clinic in Europe or the West. Onchocerciasis and trachoma are the major exceptions.

XVII. Primary glaucoma

We come to the last of our subdivisions of eye disease in Africa, namely glaucoma. This condition we found sporadically wherever we went, but it was very noticeable that it tended to appear in vast numbers in certain restricted areas. The typical appearance was a quiet eye with slightly raised tension (30 to 40 mm. Hg) and deep glaucomatous-type cupping. It was never seen in a congestive stage; only rarely did we find bedewing. The angles as viewed by the Goldmann gonioscope were wide and open.

It is difficult to explain why so many of these cases were located in two particular areas in West Africa, namely Okene in the Kabba province of north Nigeria, and Banso in the highlands of the south Cameroons. We attempted to find a toxin in the diet, thinking particularly of argemone oil, sanguinare, and citral. However, although the Mexican poppy is found in this part of the world and is used in the diet in places, in these two districts it was used probably least of all. We could get no lead on sanguinare.

In the case of citral poisoning one would have expected to have found—if citral is in fact a cause of glaucoma—many more cases in the high forest regions of east Nigeria (which we visited for a month) than in the highlands of the south Cameroons or even in the Kabba province, which is in the transitional zone, the middle belt, between the scrubland and the citrus belt. This was not the case.

We spent a lot of time on this problem, but in the circumstances we could do little else other than touch on it, and record where glaucoma was most common. As a cause of blindness, of course, this disease must rank

fairly high, inasmuch as it is insidious in onset and complete and bilateral.

Conclusions

In the territories of northern Ghana, northern Nigeria, the northern Cameroons, and the highlands of the southern Cameroons, the incidence of blindness ranges from 0.5 to 3.0 percent. The highest incidence was found in the northern territories of Ghana and the lowest in the highlands of the southern Cameroons. There are in these three countries somewhere in the neighborhood of 400,000 blind people. The heaviest area of endemic onchocerciasis was in the northern territories of Ghana where out of a million people our estimate is that 600,000 of them suffer from the disease; of the 30,000 blind here we consider that 18,000 have been blinded by onchocerciasis. There must be about 200,000 blind alone in the areas we visited.

Taking this part of Africa as a whole, the principal causes of blindness are trachoma, the purulent keratides (that is, smallpox, measles, and so forth), and senile cataract. Where onchocerciasis is endemic, the chief cause varies according to the density of the infestation by the parasite: in the northern territories of Ghana where the density is high ocular onchocerciasis is the chief cause of blindness; in north Nigeria and the Cameroons it is the chief cause only in certain small areas.

It would seem that, in addition to the formulation of a program to eradicate the fly vector of onchocerciasis and to control the human reservoir in endemic areas, if this terribly high rate of blindness is to be reduced, our effort should be directed against such diseases as syphilis, tuberculosis, smallpox, and measles. In short, the prevention of blindness in Africa must first of all be approached from the point of view of the public health services.

It is sad in this day and age that so many inhabitants of the earth are unfortunate enough to be short of such an essential vitamin as is vitamin A. The nutrition of these people suffers and, as has been indicated in this paper, the deficiency of vitamin A certainly appears to reduce the resistance of the ocular tissues to other infections; in many instances, too, it gives rise in itself to ocular lesions.

Multiple infections and deficiencies are more often than not the rule; for example, in one instance we had a patient with phlyctenulosis of the eye who in addition had onchocerciasis, loaiasis, bilharzia, and trypanosomiasis. His diet was deficient in vitamin A, protein, riboflavin, and even in calories. As long as such a situation is allowed to continue, there is no hope of reducing the rate of blindness in these territories.

There is an extremely great need for qualified ophthalmologists in every territory in Africa, and there is a surprising lack of research into tropical ophthalmology. In this respect, there come readily to mind the terrific potentialities awaiting the arrival of a glaucoma team in a place like Okene, an onchocerciasis team in Navrongo, or a trachoma team in Katsina or Kano. While the government ophthalmologists in these territories carry out good work, it is obvious that they are going to be largely bound to routine clinical duties in the main towns. That is their job. In northern Nigeria there are four ophthalmologists, three being missionaries, for 16 million people.

Now that the extent of the task is known and the causes of blindness in the different regions understood, there clearly remain two things:

1. There has to be prosecution of clinical research into such tropical eye diseases as ocular onchocerciasis with a view to preventing blindness. I believe this must take place from our highly geared research institutes in the west, for a laboratory background is essential.

2. Treatment of the huge number of eye

cases needing surgical or medical care. The incidence of eye disease in Africa bears a much higher relationship to the incidence of blindness than it does in Europe. While, in tropical countries especially, prevention is always the best line of approach, great and immediate relief can be given by the old methods of surgery and medicine. For this, Africa needs help. Africans themselves must get on with improving their public health services.

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RETINAL ARTERIOSPASM IN POLYCYTHEMIA VERA*

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Circulatory disturbances in the eye often occur in polycythemia. According to Walsh,[1] the chief eye symptoms in this disease are: (a) hyperemia of the conjunctiva, (b) dilatation of the retinal veins and sometimes of the retinal arteries as well, and cyanosis of the fundus, (c) hyperemia or edema of the disc, (d) optic nerve atrophy, (e) retinal hemorrhage, (f) perivasculitis along the veins, (g) central vein thrombosis, and (h) retinal arteriospasm.

Retinal arteriospasm is a very uncommon symptom in polycythemia vera and has hitherto been described in only four cases. We have had the opportunity of making a detailed study of an additional case.

Case report

A. E., a woman, was born in 1907. Primipara, normal parturition in 1929. In 1944, acute, transient loss of vision in left eye for two to three minutes. In 1945, she started to have attacks of blanching or cyanosis of the fingers, accompanied by numbness and paresthesia. In 1947, sweating and flushing were superadded; menstruation was regular, as earlier. In October of this year, she had repeated attacks of complete loss of vision in the left eye, of the same nature and duration as in 1944. She was admitted to the Eye Clinic, Karolinska Sjukhuset.

Examination between two attacks showed completely normal conditions in both eyes. During an attack, the left fundus exhibited very narrow arteries, macular edema, and slight hyperemia of the disc. One of these attacks was photographed and published.[2] In the intervals between the attacks the electroretinogram (ERG) was normal. Each attack of loss of vision lasted two to three minutes. For the first few hours they occurred about every 15 minutes, and thereafter at intervals of two to three hours. After 24 hours, the attacks ceased.

The eye disease was interpreted as arteriospasm of unknown origin. The following can be mentioned from investigation in 1947: Hgb. 15.8 gm./100 cc., RBC 4.8 million, WBC 11,800. In the peripheral WBC there was a shift to the left with two percent metamyelocytes. Oscillometry of the arms and legs showed normal discharges.

The patient was asymptomatic until the summer of 1955, when headaches frontally and around the eyes started. On October 23rd, she had acute at-

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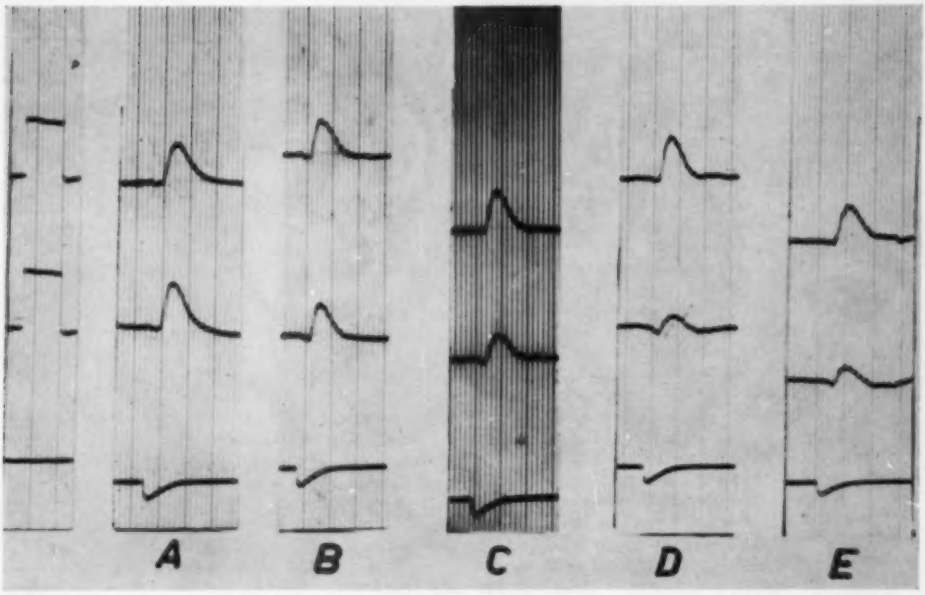

Fig. 1 (Nilsson, Rendahl, and Strömberg). Course of the illness followed by electroretinography. Uppermost curve: Electroretinogram of right eye. Middle curve: Electroretinogram of left eye. Bottom curve: light stimulus. Time marking: 0.02 and 0.10 sec. To the left: calibration 0.50 mV. Right eye: subjectively and objectively normal. (A-E) Electroretinogram normal. Left eye: (A) October 24, 1955. Normal electroretinogram during attack-free period in beginning of illness. (B) October 25, 1955. Fundus: perimacular arteriospasm, central edema. Electroretinogram neg.+. (C) November 1, 1955. Fundus: appearance as in embolism of retinal artery. Electroretinogram neg.—. (D) November 3, 1955, Fundus: exacerbation: edema and hemorrhages. Electroretinogram neg.— (worse). (E) November 16, 1955. Visual acuity: perception of light. Fundus: arteries somewhat narrow, veins slightly dilated. Disc pale. Electroretinogram neg.— (improved).

tacks of loss of vision of the same type as in 1947. She was admitted to the Eye Clinic, Karolinska Sjukhuset.

October 23, 1955. Ophthalmologic examination between two attacks: right eye, visual acuity 1.0. Media and fundus normal. The condition of this eye continued to be unaffected throughout the whole course of the illness. Left eye: visual acuity scarcely 1.0. Media clear. The fundus had somewhat narrow arteries; the veins were wider than in the right eye. The disc was slightly hyperemic.

Examination during attack: right eye unchanged. Left eye: visual acuity less than 0.1. Fundus: arteries very narrow, veins greatly dilated. The attack lasted for about three minutes. As in 1947, the condition was interpreted as arteriospasm of unknown origin. Vasodilator medication was given tentatively in the form of retrobulbar injection of Priscol®, as well as papaverine and Regitin®, orally.

October 24th. Renewed attacks, with same retinal picture as on previous day. Electroretinographic examination (figs. 1 and 2) was made in order to record one of these attacks; the right eye was normal and the left eye was also normal between the attacks. During examination, there was sudden loss of vision in the left eye. The first electroretinogram was recorded about one minute after the attack started and was definitely pathologic (neg. —) (See fig. 2). The electroretinogram remained unchanged for five minutes; vision then returned and the electroretinogram was normalized within two minutes.

October 25th. Left eye considerably worse. Visual acuity: hand movements in front of the eye. Fundus: macular edema with arteriospasm in the surroundings. The veins were dilated and there was hemorrhage upward and nasally in the fundus. Electroretinogram: neg. + (fig. 1).

November 1st. No attacks of loss of vision had occurred in the past few days. Left eye: visual acuity was finger counting at three meters peripherally. Fundus: macular edema with cherry-red spot; fresh small hemorrhage beside the macula. Electroretinogram: neg. — (fig. 1).

November 3rd. On waking, the visual acuity of the left eye was greatly decreased, being con-

fined to hand movements peripherally. Fundus: marked edema, arteries greatly contracted, segmented columns of blood in arteries and veins. Electroretinogram: neg. — (fig. 1).

November 7th. The condition was largely unchanged, except for slightly less contraction of the arteries. The electroretinogram was somewhat improved but was still neg. —.

November 18th. The patient was discharged; the condition of her eyes was unaltered.

Blood counts: Hgb. 14.2 gm./100 cc., RBC 4.5 million, WBC 8,300, differential count normal. S.R. 2.0 mm./1.0 hr. X-ray examination of the orbits and skull showed normal conditions, as did the electroencephalogram. Oscillograms of the arms and legs showed normal discharges.

During November and December, 1955, the state of the left eye gradually improved. The vessels resumed their normal width, the hemorrhages became resorbed, and the edema subsided (fig. 3), but the visual acuity did not increase.

The patient was referred to the Endocrinologic Clinic, Serafimerlasarettet, for further investigation. In January, 1956, the blood counts were: Hgb. 17.9 gm./100 cc., RBC 5.8 million, WBC 6,000, differential count normal. S.R. 1.0 mm./1.0 hr. The patient did not return for investigation until the fall of 1956. During the spring and summer she had suffered from conjunctivitis, which did not respond to topical administration of cortisone. In June, 1956, the state of her eyes was practically the same as in the previous December, except that there was distinct pallor of the left disc. In September she was admitted to the Endocrinologic Clinic for further investigation.

Examination on admission. Florid complexion and very faint cyanosis. Height 159 cm., weight 55.3 kg. Blood pressure 145/80 mm. Hg. The spleen was palpable directly below the costal margin; the liver was not palpable. The blood laboratory data were as follows. RBC 5.7 to 5.9 million/mm.[3] Thrombocytes 350,000–400,000/mm.[3] Hgb. 18.8 to 19.7 gm/100 cc. Total Hgb. 814 gm. (calculated normal value 420 gm). Total blood cell volume 43.3 cc./kg. Plasma volume 31.1 cc./kg. Hematocrit 59 percent. Arterial oxygen saturation 92.8 percent. Sternal puncture: hyperplasia of all cell forms. Serum iron 56 gamma percent. Fe^{59}-½ T 40 min. (normal range 70 to 140 min.).

The Fe^{59} determinations were made according to Huff et al.[5] The total hemoglobin was determined by the alveolar CO_2 method (Sjöstrand[4]). The differential white cell count showed a shift to the left, with one to two percent metamyelocytes and myelocytes. The patient also had "giant thrombocytes" in the peripheral blood.

Other examinations gave the following results: S.R. 1.0 mm./1.0 hr. Serum uric acid 3.9 mg/100 cc.

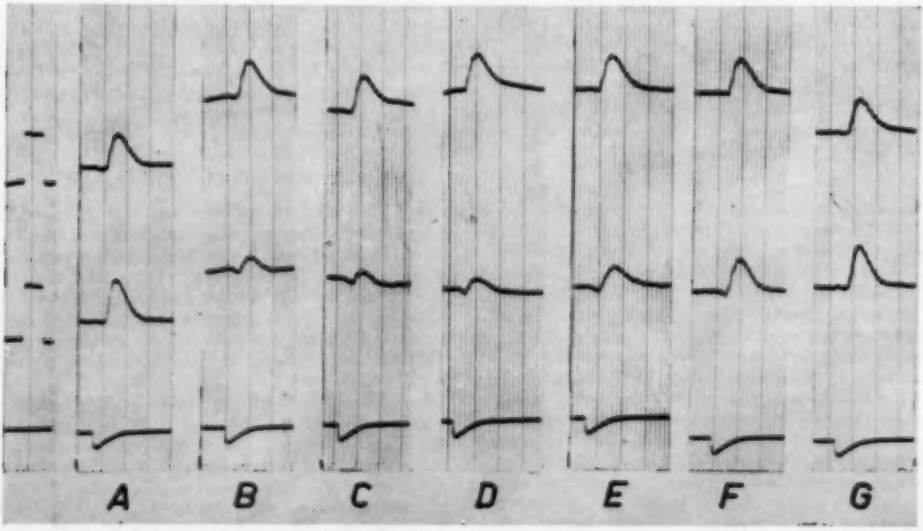

Fig. 2 (Nilsson, Rendahl, and Strömberg). Electroretinogram during an attack of retinal arteriospasm. Arrangement as in Figure 1. Right eye: Electroretinogram normal. Left eye: (A) Before attack. Subjectively, visual acuity normal. Electroretinogram normal. (B) Two minutes after beginning of attack. No vision in left eye. Electroretinogram neg.—. (C and D) Five and one-half and six minutes after beginning of attack. Subjectively, status quo. Electroretinogram neg.—. (E) Fifteen seconds later vision has returned. Electroretinogram neg.—. (F) One-half minute after return of vision. Electroretinogram neg.+. (G) Two minutes after return of vision. Electroretinogram normal.

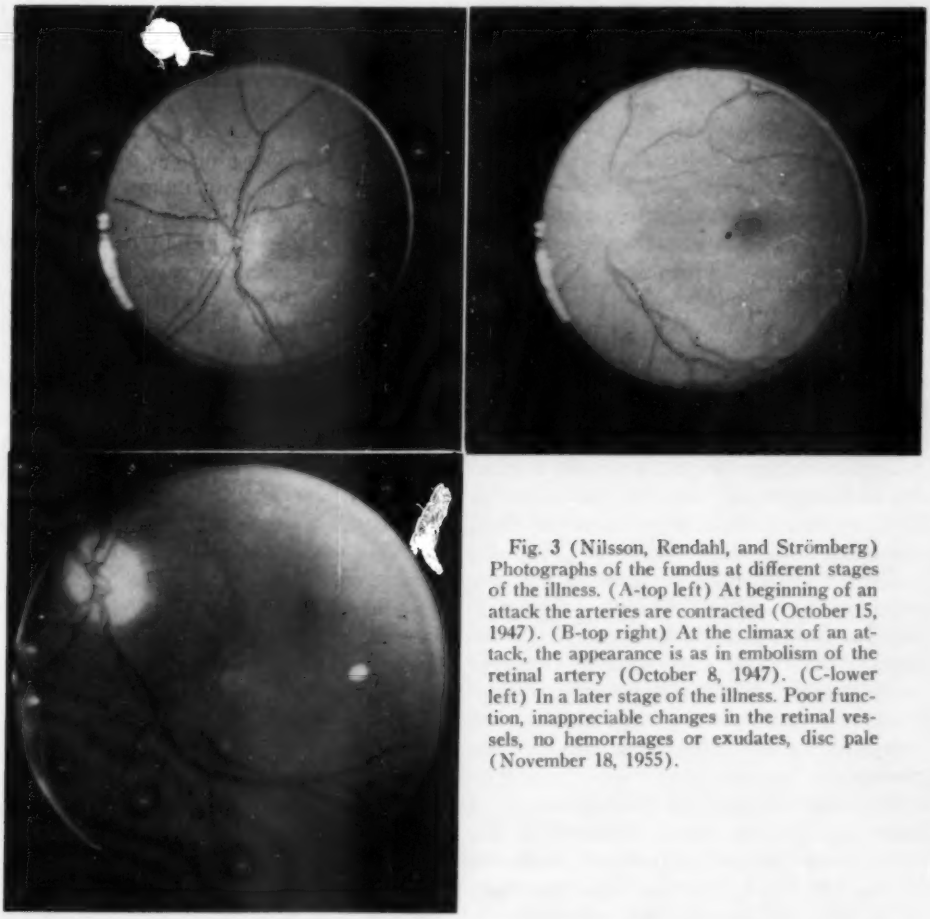

Fig. 3 (Nilsson, Rendahl, and Strömberg) Photographs of the fundus at different stages of the illness. (A-top left) At beginning of an attack the arteries are contracted (October 15, 1947). (B-top right) At the climax of an attack, the appearance is as in embolism of the retinal artery (October 8, 1947). (C-lower left) In a later stage of the illness. Poor function, inappreciable changes in the retinal vessels, no hemorrhages or exudates, disc pale (November 18, 1955).

Fractionated protein with albumin 4.8 percent, globulin 2.1 percent, and normal electrophoresis. Nonprotein nitrogen 35 mg./100 cc. W.R. negative. X-ray examination of the skull and orbits showed normal conditions. X-ray examination of the spleen disclosed moderate enlargement. There were no roentgenologic abnormalities of the heart, lungs, or liver. The electroencephalogram was normal. Oscillometry of the extremities showed normal discharges. Hormone analyses on the urine: 17-ketosteroids 9-11 mg./24 hr., corticosteroids 26-32 mg./24 hr., gonadotropins $>$ 40 mEq/24 hr., noradrenalin 1.4μg., adrenalin 2.6 μg/24 hr.

Ophthalmologic examination on November 16, 1956: right eye normal. Electroretinogram, normal. Left eye: perception of light. Fundus: disc pale, arteries somewhat narrow, a few veins slightly dilated with variations in caliber. Electroretinogram, neg. — (fig. 1).

Discussion

In the fall of 1956, the patient exhibited relatively few symptoms, although the laboratory data showed all the changes characteristic of polycythemia vera (Lawrence[5]). Thus she had a raised red cell count, an increase in total hemoglobin, and a disproportionately raised iron metabolism. The normal arterial oxygen saturation, bone-marrow hyperplasia, increase in the number of thrombocytes, and enlargement of the spleen also argued in favor of this diagnosis.

The most conspicuous features, in addition to the fundus changes, were the attacks of

cyanosis of the fingers, accompanied by paresthesia and numbness, as well as severe, persistent headache, localized to the forehead and around the eyes. This form of cyanosis, known as Raynaud's phenomenon, as well as persistent headache, are not infrequent in polycythemia.

The normal arterial oxygen saturation and absence of any pathologic changes in the circulatory organs and lungs ruled out the presence of secondary polycythemia. Investigation also failed to disclose signs of any other disease (collagenosis, arteriosclerosis, intraorbital tumor, brain tumor, or epilepsy) that could be responsible for the symptom complex.

Ophthalmologic symptoms of the nature described can be attributed to the patient's polycythemia, and no grounds existed for any other cause of the eye disease.

The eye symptoms were similar at examination in 1944 and in 1947, and on the latter occasion it was possible to observe and photograph the retinal arteriospasm. Although no thorough medical investigation was made on these occasions, it is probable that an increase in the red cell volume was already present.

The vascular changes in the fundi in polycythemia vera are usually localized to the veins. Only four cases of spastic conditions of the retinal arteries have been described. It is true that patients with polycythemia vera are often known to suffer from transient loss of vision in one eye and, as early as 1906, Köster[6] assumed this symptom to be due to transient arteriospasm. However, in his opinion, spasm of the cerebral arteries was presumably responsible for the loss of vision. Brown and Giffin[7] described 14 cases of polycythemia vera with fundus changes: five of them had stasis of the retinal veins and contracted arteries. The arterial changes were interpreted as arteriosclerotically conditioned, and were not considered to be related to the blood disease.

Mylius[8, 9] was the first to make detailed observations and to photograph spasm of the retinal arteries in polycythemia vera. In this case, only one eye was affected; this also applied to one case reported by Lisch[10] and two by Nagy.[11]

The etiology of arteriospasm in polycythemia vera is unknown. In some cases arterial lesions are present, with intimal thickening and fibrosis of the adventitia (Retznikoff et al.[12]). In the case described by us, there was no evidence of organic vascular lesions; consequently, the fundus changes must be regarded as functionally determined. Support is lent to this interpretation by the electroretinographic examinations made in the course of the illness in 1955.

Electroretinography provides a good idea of the functional ability of the retina (Karpe[13]), whereas the electroretinogram is unaffected by damage to the optic nerve. The electroretinogram is greatly influenced by circulatory disturbances, and the positive b-potential recorded decreases in size (subnormal electroretinogram) or is preceded by a negative a-wave (negative + electroretinogram). If both a decrease in the b-potential and an a-wave are present, the curve is denoted as negative−. In total occlusion of the central retinal artery, an extinguished electroretinogram is recorded in advanced cases (Karpe,[13] Henkes,[14] Karpe and Uchermann,[15] Heck[16]).

In the present case, a normal electroretinogram of both eyes was recorded during an attack-free period in the early stage of the disease (fig. 1). This argues against an organically determined, severe circulatory disturbance in either eye. During a temporary loss of vision, the electroretinogram deteriorated rapidly (fig. 2) and after one minute a typical, neg.− electroretinogram was seen. When the arteriospasm had subsided after a few minutes, vision returned to normal and the electroretinogram was completely normalized within two minutes.

The observations made confirm the sensitivity of the retina to circulatory disturbances, and also show how rapidly restitution can take place after brief, almost total in-

terruption of the circulation in the retinal arteries. Similar events have been studied in animal experiments by Granit,[17] Bornschein and Zwiauer,[18] Noell,[19] and Popp,[20] among others.

During the subsequent course of the disease, irreversible damage to the retina occurred, with a concomitant, gradual deterioration of the electroretinogram. Initially, the damage was confined to small areas in the central parts of the retina. At that time, the electroretinogram was still practically normal, that is, neg.+ (fig. 1). Later, in association with an increased state of contraction in the central retinal artery, more widespread fundus changes appeared. This was accompanied by a deterioration of the electroretinogram, which was then of the characteristic neg.— type. To the extent to which regression of the arteriospasm could be observed thereafter, some improvement in the electroretinogram was noted. The first change was a slight increase in the size of the b-potential, followed by decreased negativity. This implies that retinal damage had occurred in the course of the illness, and had produced an irreversible change in the electroretinogram, which could no longer become normalized despite improved circulation.

Summary

1. Retinal arteriospasm in polycythemia vera has earlier been described in only four cases. An account is given in this paper of an additional case.

2. The patient was examined for the first time in 1947, owing to rapidly transient attacks of retinal arteriospasm, associated with temporary loss of vision, in one eye. Investigation then gave no grounds for suspecting a systemic disease and the condition was diagnosed as arteriospasm of unknown origin. One attack was photographed and published.[2]

3. After an asymptomatic period, the eye symptoms returned in 1955. Initially, they were in the same form as earlier, that is, transient, unilateral arteriospasm. Lengthy arterial contraction supervened, and caused permanent retinal and optic nerve damage. Both an attack in the initial stage of the illness and the various phases of the later course were followed by electroretinography. The patient was referred for endocrinologic investigation, and polycythemia vera was diagnosed in 1956.

4. It is pointed out that earlier investigations have indicated a purely functional cause of the retinal arteriospasm. The electroretinographic study of the present case is regarded to confirm the primary absence of any organically determined circulatory disturbance. No definite explanation of the vasoconstriction is found.

Karolinska Sjukhuset (60).

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RETINAL ARTERY BLOOD PRESSURE CHANGES*

With compression or ligation of the carotid arteries

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A relatively simple method of estimating retinal artery blood pressure (ophthalmodynamometry) has been known for many years. Although the reliability of the method in measuring absolute values has not been settled, there is excellent clinical evidence to support the validity of the measurements in determining relative pressures in the two eyes. The retinal artery blood pressure may be assumed to be of the same order as the pressure in the internal carotid artery on the same side since the ophthalmic artery is the first branch of this vessel. Thus, a convenient method of comparing blood pressure in the two internal carotid arteries is available.

Recognition of the diagnostic value of the retinal artery blood pressure in cases of occlusion of the carotid system has recently stimulated interest in its use. Our clinical and surgical experiences in these cases will be the subject of a separate paper.[1] We would like here to discuss the effect of manual compression and surgical ligation of the carotid arteries on the blood pressure of the ophthalmic arteries.

The standard technique of ophthalmodynamometry was applied. We used the dynamometer of Müller. Only the direct plunger readings are given in our tables. The intraocular pressure was within normal range in all the patients described in this paper.

I. Change in retinal artery pressure on digital compression of the common carotid artery

We have measured retinal artery blood pressure in 10 patients, free of apparent arterial disease and vascular insufficiencies, for the purpose of determining the effect of firm digital compression of the common carotid artery. All the retinal artery pressure determinations were made by the same observer (F. B.).

Control measurements were first taken with the subject at rest in the supine position. Then, while the common carotid artery was being digitally compressed to the degree of intended complete occlusion on one side, measurements in each eye were taken.† If

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† We noted in several of the patients under study that what seemed to be adequate digital pressure over the common carotid artery did not at first result in a change in ipsilateral retinal artery pressure. In an effort to make the maneuver of percutaneous occlusion more effective we found that digital compression of the common carotid can be most reliably performed by the use of both hands. With the patient supine the operator stands on the side to be compressed. The fingers of one hand are placed behind the neck over the paraspinal muscles on the same side and moderate force is exerted upward to increase the lordosis of the cervical spine and to prevent movement during compression. It is important that the sternocleidomastoid muscle be relaxed. The fingers of the other

TABLE 1

INFLUENCE OF UNILATERAL PERCUTANEOUS DIGITAL COMPRESSION OF THE COMMON CAROTID ARTERY ON RETINAL ARTERY PRESSURES

Age (all male)	Neurologic Diagnosis	Initial Pressures Systolic/Diastolic Right Eye	Initial Pressures Systolic/Diastolic Left Eye	Compression of Right Common Carotid Artery Right Eye	Compression of Right Common Carotid Artery Left Eye	Compression of Left Common Carotid Artery Left Eye	Compression of Left Common Carotid Artery Right Eye	Brachial Arterial Blood Pressure (mm. Hg)
J.W., 35	Psychomotor epilepsy	70/38	66/32	40/24	84/38	30/22	80/42	115/75
D.K., 32	Sciatica	82/38	72/32	38/0*	60/26	38/0*	82/28	136/64
D.S., 23	Idiopathic epilepsy	80/42	82/32	52/28	60/34	44/28	82/44	96/64
E.N., 24	Encephalopathy post-traumatic	74/36	74/32	42/28	84/22	50/28	84/68	126/68
D.A., 37	Aneurysm right internal carotid (intracranial)	80/26	82/38	22/16	82/42	36/20	84/44	116/42
W.F., 51	Encephalopathy, chronic alcoholism	110/65	105/66	40/18	110/55	35/25	95/50	126/36
K.S., 33	Idiopathic epilepsy	110/68	100/55	82/52	125/60	75/48	120/75	126/36
R.J., 38	Focal epilepsy, local atrophy, right frontal-parietal	95/42	100/55	28/2*	125/65	25/0*	—	122/36
J.S., 30	Idiopathic epilepsy	103/75	112/75	53/33	120/92	55/36	120/75	142/96
L.W., 28	Idiopathic epilepsy	84/32	76/36	32/16	76/46	42/30	84/52	106/68

Intraocular pressures within normal limits and essentially equal in the two eyes in all cases.
* A reading of zero or near zero implies an arterial pressure approximately equal to the intraocular pressure.

the subject was free of any significant symptoms due to the compression, the carotid artery on the opposite side was independently compressed and measurements taken again. The three sets of readings were completed within a period of five minutes.

Examination of Table 1 and Chart 1 will show that in all subjects a substantial drop in either systolic or in both systolic and diastolic retinal artery pressures followed digital compression of the common carotid artery on the same side. Pressures in the eye on the side opposite to that of compression were, as a rule, slightly increased. This latter finding has also been reported by Baurmann,[2] Heyman, Karp, and Bloor,[3] and Brackett and Mount.[4] A pronounced fall in pressure was associated with symptoms of ischemia in two patients.

Repeated application of pressure to the eyeball within a period of five minutes might reduce the ocular tension and thus introduce an error in the comparative and uncorrected readings. We believe that such a possible error was not significant in the interpretation of our measurements since prolonged pressure on the eye was avoided.

The percentage drop for both right- and left-sided compression averaged together was 51 for the systolic pressure and 49 for the diastolic. In view of the considerable range of these percentage falls throughout the 10 cases, the average is of doubtful value.

Miletti (1946)[5] made similar studies by digitally compressing a common carotid artery in 30 normal subjects. The diastolic pressure in the ipsilateral retinal artery dropped more than 50 percent while the systolic pressure dropped less than 50 percent. In a few subjects he detected no change in retinal artery pressure. He noted a tendency for the reduced pressure to increase when compression of the carotid artery was sustained for three minutes.

COMMENT

While an extensive comparative study of retinal artery pressure determinations by

hand can then easily palpate the pulsating artery and by downward pressure compress it against the spine until pulsation beneath the fingers ceases. It is possible that the carotid bulb as well as the common carotid artery may be thus compressed in some patients.

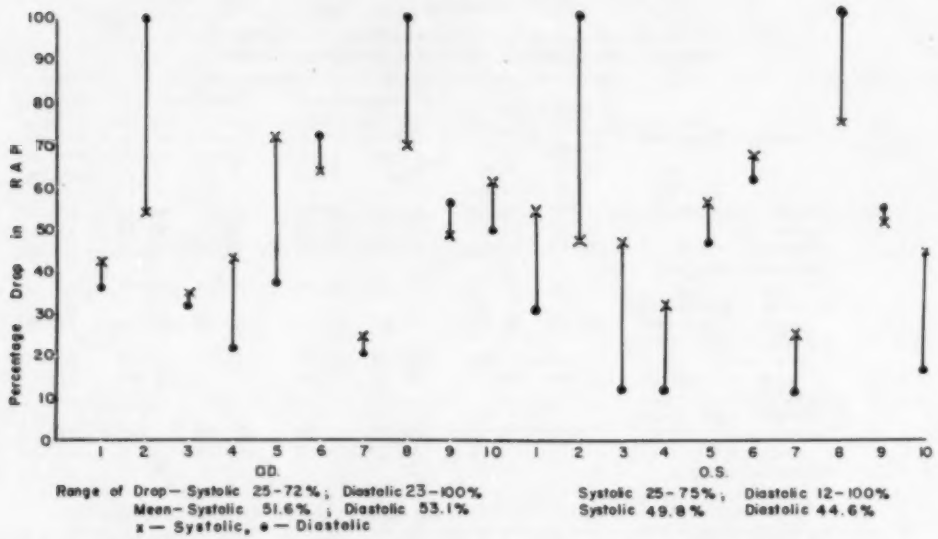

Chart 1 (Van Allen and Blodi). The influence of digital compression of the common carotid artery on the numerical values of ipsilateral retinal blood pressure is shown in Table 1. This chart illustrates the percentage changes in the same patients.

ophthalmodynamometry and simultaneous intracarotid pressure readings is as yet not available, Rand[6] has shown a rather close correlation. Natural limitations of the method and of the ophthalmodynamometer itself will not provide great accuracy in the measurement of absolute pressures but the practical importance of comparing relative pressures seems well established.

Our studies of blood pressure fall in the ophthalmic arteries after compression of the common carotid may be compared with studies of directly measured pressure in the internal carotid artery distal to its occlusion.

Sweet, Sarnoff, and Bakay[9] after clamping the internal carotid or the common and external carotids in 39 subjects found the average percentage fall in systolic pressure in the distal internal carotid to be 49; the average percentage fall in diastolic pressure was 34, and the average fall in the pulse pressure was 69 percent. In respect to variability and degree of response our determinations of the drop in systolic pressure in the retinal artery after digital compression of the common carotid artery were of the same order as reported by these authors. Our determinations of the percentage drop in diastolic pressure, however, were more variable from patient to patient and were greater in degree.

Our compression experiments have reconfirmed the influence of manual compression of the common carotid on the blood pressure in the ophthalmic arteries. This experimental evidence has to be kept in mind when evaluating and following the effects of a surgical ligation of one carotid artery.

II. Ophthalmodynamometry in ligation of the carotid arteries

The hazard of carotid ligation has prompted considerable study of means for predicting which patients will tolerate direct ligation and which may require preliminary partial ligation or the use of an adjustable arterial clamp. The consideration of whether to ligate the common or internal carotid artery in a given case is part of this problem.

Johnson[7] found, in a study of direct measurement of pressure in the internal carotid,

that when proximal occlusion caused a drop in pressure of over 60 percent three of five such patients developed hemiplegia in a trial period of 30 minutes. He suggested that pressure studies could be of value in judging which patients should have preliminary partial ligation. However, he pointed out that pressure studies are not an accurate index of the blood flow.

Miletti and DiLuca[8] stated that ligation of the internal carotid artery is not safe if retinal artery pressures drop below 50 percent on the side of the arterial occlusion.

Rand[6] has recently stated that gradual progressive occlusion of the carotid artery is indicated if systolic or mean retinal blood pressures decline 55 percent or more on performance of the Matas test ipsilaterally.

Sweet, Sarnoff, and Bakay[9] in a series of cases studied by direct pressure methods concluded that a pressure drop in the distal internal carotid artery after occlusion to 30 percent of the original level (that is, a drop of 70 percent) indicated that ligation is hazardous. Two of the three deaths in their series were associated with pressure falls of this magnitude. Since the individual response to ligation is so variable, they suggest that preliminary pressure studies should be done in all cases.

The report of Strobos and Mount[10] indicates a similar experience:

Most of the complications of various carotid ligations occurred when pressure in the internal carotid artery showed a fall of 70 percent or more in systolic readings. Their direct pressure measurements were combined with interpretation of carotid flow derived from angiographic studies. They emphasized that although pressure studies are of some value, they are not completely reliable in predicting tolerance of carotid ligation. It would appear that, while a marked drop in pressure in the internal carotid artery distal to occlusion is a valuable warning sign, a less dramatic drop does not insure safety of ligation.

Lobstein and co-workers[11] have reported comparative studies of retinal blood pressure and carotid arterial pressure in patients treated by carotid ligation for intracranial aneurysms and vascular anomalies. They concluded that retinal artery pressure measurements are of value in determining the effectiveness of carotid ligation and in judging the extent of ligation compatible with adequate circulation.

The ideal of accurate direct pressure readings can not be realized by all who do surgery on the carotid system. Retinal blood pressures which reasonably parallel the findings of direct pressure measurements are possible to all who care to perfect the technique. Moreover, direct pressure readings are neither easily obtained repeatedly in the same patient nor for many hours after operation. There is definite value in information in respect to the development of collateral circulation for a period of days or weeks after ligation. This information has application in the case of congenital intracranial aneurysm when rising internal carotid pressures after a carotid ligation might be regarded as an indication for further arterial occlusion to safeguard the weakened vascular wall.

Retinal artery pressure studies could also be of value in following the case in which preliminary therapeutic ligation of the common carotid has been done. A satisfactory rise in pressure could possibly indicate a safe time to ligate the internal carotid artery when that seemed desirable.

Svien and Hollenhorst[12] report two cases in which common carotid ligation was tolerated but diastolic retinal pressures on the operated side had fallen to 50 mm. Hg as contrasted with 95 mm. Hg on the contralateral side in one patient and to 30 mm. Hg as contrasted with 80 in the other (pressure differences of 47 and 62 percent respectively.) Neither patient could tolerate subsequent ligation of the internal carotid.

Heyman, Karp, and Bloor[3] have noted other interesting applications of ophthalmodynamometry. One patient did not demon-

strate a significant fall in retinal artery pressures after carotid ligation in the neck. Arteriography disclosed that ligation was not complete. Four patients were studied while a common carotid artery was being gradually occluded by a Crutchfield clamp. The degree of fall in retinal artery pressure was roughly proportional to degree of arterial occlusion. In one patient the retinal artery pressure rose unexpectedly to previous levels. It was found that the clamp had been released.

The following case illustrates several of these applications to problems related to occlusion of the common carotid artery.

Case report

D. A. (28486). This white man, an electrician, was first admitted to the Veterans Administration Hospital, Iowa City, on January 12, 1954, at the age of 34 years. During the preceding two months he had suffered several sudden bouts of severe sharp pain above the right eye, followed by steady and nagging pain in this area. For one month there had been diplopia. A lumbar puncture done elsewhere after an acute attack of pain had not shown the presence of blood.

Physical examination disclosed no abnormal findings. The blood pressure was 110/80 mm. Hg. On one occasion compression of the right common carotid artery gave relief of pain. Ophthalmologic examination yielded findings suggestive of weakness of the right superior and inferior rectus muscles. Routine laboratory studies including spinal fluid findings were not abnormal. The symptoms cleared rapidly and the patient returned to work.

He was readmitted on February 10, 1954, soon after discharge, because of recurrent pain in the right forehead. There were no new physical findings. It was found that compression of the right common carotid artery caused immediate complaint of lightheadedness and blurring of vision. Right carotid angiography was done by open technique in order that we might obtain information about collateral flow. An intracranial aneurysm of the right internal carotid just proximal to its bifurcation was visualized. It was elected to treat this by ligation of the common carotid artery but a small abscess was found in the wound when it was reopened for this purpose nine days later. Again symptoms abated and because compression of the artery in the neck regularly caused symptoms of ischemia in five to 10 seconds, nothing further was done over a period of 30 months during which time he was seen at frequent intervals and was relatively asymptomatic.

He was hospitalized again on January 11, 1957, because of recurrence of severe right frontal pain and inconstant blurring of vision. The wound of the neck was well healed and carotid artery pulsations in the neck were strong on both sides. There were no significant physical findings. Routine laboratory studies and roentgenograms of skull and chest were within normal limits. Again it was noted that digital compression of the right common carotid artery in the neck resulted in "dizziness" and blurring of vision. This was repeated on successive days and tolerance to the maneuver developed so that finally he could endure three minutes of such compression without symptoms. The resting electroencephalogram showed only slight diffuse abnormalities and carotid compression for three minutes on either side produced no further abnormalities.

Retinal artery pressure studies were done in the presence of systemic blood pressure of 116/42 mm. Hg and normal and equal intraocular pressures. The readings were: O.D., 80/26; O.S., 82/38 gm. Digital compression of the right common carotid artery resulted in these readings: O.D., 22/16; O.S., 82/42 gm. Compression on the left: O.D., 84/44; O.S. 36/20 gm. After it was found that the patient could tolerate digital compression of the common carotid artery on the right, ligation of the artery was planned.

Operation was carried out on January 24, 1957. Papaverine was administered. The right common carotid artery and its branches were exposed under local anesthesia. The vessels were normal except for early atherosclerotic changes. Preliminary retinal artery pressure readings were: O.D., 80/32; O.S., 80/40 gm.

Occlusion of the right common carotid artery by clamp caused the same profound drop in retinal artery pressures produced by percutaneous compression. After clamping the right common carotid the readings were: O.D., 20/10; O.S. 84/44 gm. However symptoms were minimal. Several combinations of arterial clamping were studied but of particular interest was the fact that clamping of the right internal carotid alone resulted in retinal artery pressures of: O.D., 50/22, and O.S., 84/50 gm. When the external was clamped in addition, the pressures were: O.D., 20/10; O.S., 84/60 gm.

The retinal artery pressure studies are summarized in Chart 2. External carotid angiograms were performed on the operating table in an effort to demonstrate collateral circulation. These were technically unsatisfactory.

The right common carotid artery was ligated. A strip of fascia lata was sewed around the artery as a cuff and a heavy silk ligature was tied down over this. Three hours after surgery the readings were: O.D., 32/20, and O.S., 76/36 gm. but four hours later the pressures were: O.D., 74/26, and O.S., 84/40 gm. This rapid rise in pressure in the right eye led to more detailed general examination. While the patient was tolerating the ligation very well, a temporal artery pulse was evident on the right and a loud bruit was audible over the region of the exploration. Slipping of the ligature was

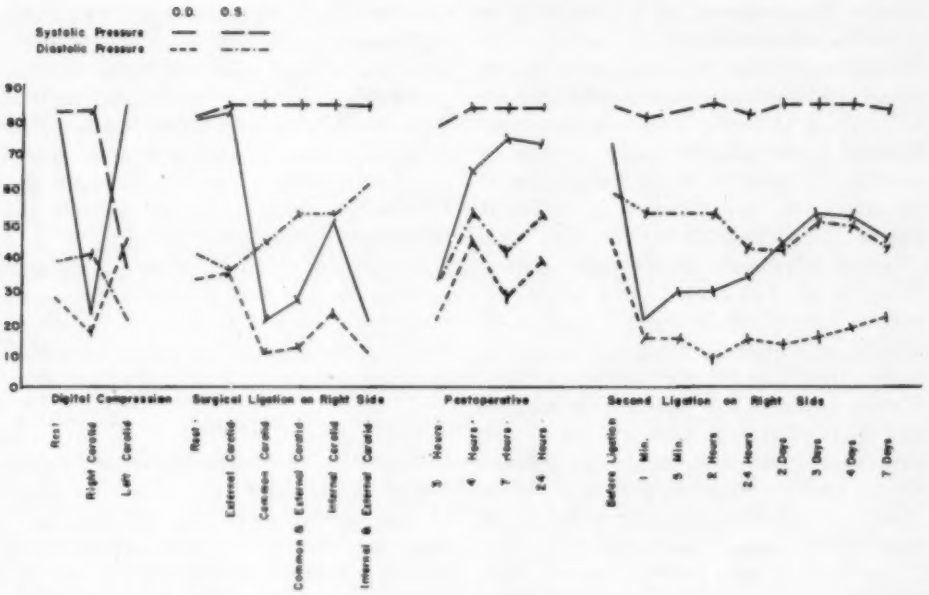

Chart 2 (Van Allen and Blodi). The changes of retinal artery blood pressure in the case reported herein are illustrated. On the left are the values before operation.

assumed, but it was decided that this inadvertent partial ligation might be an advantage to the patient and nothing was done for 24 hours. During this time and subsequently, the patient was observed closely and systemic blood pressure was maintained above 120/70 mm. Hg by orally administered ephredrine sulfate.

The bruit and temporal artery pulse on the right were still evident on the following day (January 25th) and retinal artery pressures were: O.D., 72/44, and O.S., 84/56 gm. The wound was opened under local anesthesia. A definite bruit was palpable at the site of ligation and was obliterated by clamping the common carotid artery. It was estimated that the original ligature which was still in place occluded the artery 50 percent.

Another ligature was passed around the protecting fascial strip and tied very securely. The bruit and temporal artery pulse vanished and immediate pressure readings in the retinal arteries were: O.D., 20/14, and O.S., 80/50 gm.

Following this the patient did very well. There were no symptoms of cerebral ischemia, and he was free of headache and diplopia. Complete bedrest was prolonged for five days when progressive elevation of the head and eventual ambulation were permitted. Ephedrine sulfate was used to maintain systemic blood pressures. Retinal artery pressure readings rose slowly on the right side and on February 7, 1957, the readings were: O.D., 64/36, and O.S., 115/66 gm. The common carotid artery was a hard cord and no pulse was palpable on the right side of the neck or head. He was asymptomatic when discharged the following day.

He returned to the hospital on March 7, 1957. The former headaches were absent but when he had attempted to work a week before he experienced some lightheadedness on change of position, with weakness and transient blurring of vision. There were no signs of neurologic deficit. No arterial pulsations were evident on the right side of the head and neck. The right side of the face was slightly cooler than the left. The retinal artery pressure readings were: O.D., 45/22; O.S., 115/66 gm. Light digital pressure on the right eyeball caused arterial pulsation in the retina.

Repeated brachial artery pressure determinations on the ward were found to vary from 90/65 to 115/80 mm. Hg. He was essentially symptom free on the ward and extra table salt in amounts of 20 gm. per day was administered in an effort to bolster temporarily the systemic arterial blood pressure. The blood pressure changed little although he gained five pounds in weight. He was discharged again on March 15, 1957. At this time brachial artery pressure was 120/70 mm. Hg. Retinal artery pressures were: O.D., 65/40; O.S., 110/62 gm.

Discussion

This case illustrates several interesting and potentially valuable applications of retinal

artery pressure determination. It shows, as do our experimental data, that percutaneous digital compression of the common carotid artery can be effectively performed in some patients and conversely it suggests that measurement of retinal artery pressure may be used to determine if digital compression is effective in the Matas test or in studies of collateral circulation.

Digital compression of the right common carotid in the neck caused a drop of 72 percent in systolic pressure and a drop of 38 percent in diastolic readings. There were minor symptoms of lightheadedness and blurring of vision. For these reasons ligation was approached with caution. The system was exposed and clamping of the common carotid artery resulted in a drop in retinal artery pressure nearly identical to that found after percutaneous compression.

Occlusion of the internal carotid alone caused a drop in readings from 80/32 to 50/22 gm. When the external carotid was then clamped a further very significant drop to 20/10 resulted. These findings suggested a collateral circulation from external to ophthalmic and internal carotid arteries via anastomoses in the face. This raised a familiar dilemma.

Should ligation be done so as to effect the greatest pressure drop or should consideration of safety of ligation be paramount? We could not conclude that the higher retinal artery pressure reading under these circumstances was typical of the entire internal carotid circulation on the right side nor that it represented the greatest possibility of eventual collateral blood supply to the brain.

After studies of collateral flow, we decided to ligate the common carotid artery. This was well tolerated. However, rapidly rising ipsilateral retinal artery pressure readings led us to the discovery of incomplete occlusion. The artery was again ligated. Chart 2 shows the drop of retinal artery pressures to former low levels and a slow increase in these levels with time.

Six weeks after ligation the patient had symptoms of transient blurring of vision and lightheadedness. The retinal artery pressures were not yet stable on the right, and not grossly different from the findings at four days and at one week after ligation. The face was cool on the side of ligation. It was felt that thrombosis may have extended into the external carotid system and probably into the internal carotid artery as well.

Denny-Brown[13] has noted that light finger pressure on the eyeball may easily cause pulsation in the retinal artery on the side of internal carotid occlusion. It is a simplified application of the method under discussion.

Summary

Estimation of retinal artery blood pressure can be made by the simple and safe technique of ophthalmodynamometry. There is good reason to believe that readings of pressure so determined are representative of and approximate actual blood pressure in the intracranial portion of the internal carotid artery. The measurements are of particular value in comparing relative levels of pressure in the internal carotid arteries on the two sides.

Percutaneous digital compression of the cervical carotid system produced a significant drop on the same side in either systolic or diastolic retinal blood pressure or both in all of 10 patients so tested and did so on either side. The considerable variability of percentage fall in retinal artery pressure so produced is not inconsistent with the variability found in directly measured pressure in the internal carotid artery when the common or internal carotid artery are occluded under direct vision. The percentage of blood pressure drop in the retinal arteries produced by digital compression of the cervical carotid system, when expressed as an arithmetic average, was about 50 percent for both systolic and diastolic values. This percentage drop for systolic pressures is in the same range as that reported for direct pressure readings in the internal carotid artery when the common or internal carotid are occluded proximally.

Studies of pressure in the carotid system, direct or indirect, are not as valuable as we would desire in predicting the result of proposed carotid ligation. It would seem, however, that the simple method of ophthalmodynamometry may eventually prove to yield as much practical information in this regard as direct intracarotid pressure measurements. But we must await further comparative studies of the two methods.

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Ophthalmic Miniature

"I can't leave all my patients for three solid months," said the doctor, "let Kim Ching get one of the Dutch doctors from Maccassar or Amboyna. There's a fellow at Amboyna who's quite all right." (For cataract surgery.)

The Chinese did not reply. He put more notes on the table. They were hundred dollar bills and he arranged them in little packets of ten. The wallet bulged less. He laid the packets side by side and at last there were ten of them.

"Stop," said the doctor. "That'll do."

The Narrow Corner, by W. Somerset Maugham.

IN VITRO LENS STUDIES*

I. Technique and preliminary results of maintenance of lens culture for 24 hours

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Introduction

During the course of investigating the effects of X-irradiation on ocular tissues[1] several processes were manifested concurrently during the acute phase of the trauma. These were inhibition of mitosis of lens epithelium, cellular exudation into the aqueous, adherence of cells to the anterior surface of the lens, and suppressed aqueous secretion. The severity of these processes generally increased as one increased the dose of irradiation to the level which was consistently cataractogenic. Similar, though less severe, events followed the systemic administration of a cataractogenic dose of iodoacetic acid.[2] Because of the multiplicity of the secondary effects of these agents, it was difficult to assess the significance, if any, of the role of each such damage to ocular tissues other than the lens on the ultimate development and progression of cataractous changes.

It seemed possible that in vitro lens culture might provide a means of avoiding these secondary effects, as well as studying the reversibility of the lenticular changes, and so forth. Such a technique has been developed successfully by Kinsey and co-workers[3,4] using a special culture medium.

The criteria for success in such studies included the maintenance not only of clarity and over-all glycolytic metabolism but also of mitotic activity of the lens.[3] The latter measure assumes particular importance in view of the recent findings of von Sallmann[5] of the correlation between mitotic index and rate of cataract development following irradiation. The studies by that group also showed an effect of several cataractogenic agents on the mitotic activity of lens epithelium in vivo.

The present studies have resulted in a simplified method for the successful culture of lenses for approximately 16 hours using a commercially available medium. The technique used and preliminary results of the effect of various conditions on the mitotic activity of lens epithelium are presented in this report.

Methods

Male albino rabbits recently received from the rabbitry and weighing approximately 2.0 kg. were used in these experiments. The animals were killed by intracardial air injection. A time lapse of five minutes or less occurred from the time of the air injection to the insertion of the second lens into the culture tube.

The eye was opened by a posterior approach and the vitreous carefully removed. Although the zonules were cut very carefully, an occasional small (1.0 mm.) weak spot developed during long-term cultures with some bulging of lenticular substance. In the few instances when this occurred, no effect on mitotic activity or over-all glycolysis was noted. The lenses were placed into the culture tube containing media equilibrated at water bath temperature by use of a PE90 polyethylene tubing made semirigid by a galvanized wire insert and with loop end sealed. Stainless steel and other metal loops were found to adhere to the lens cap-

* From the Department of Ophthalmology, Washington University School of Medicine, and the Oscar Johnson Institute. This research was supported in part by the USAF under Contract No. AF 18(600)-1269; monitored by the USAF School of Aviation Medicine, Randolph Field, Texas.

TABLE 1

COMPOSITION OF MEDIA

Ingredients	TC199 mg./liter	KEI No. 2* mg./liter
Inorganic		
Potassium carbonate	—	326
Sodium bicarbonate	2,200	2,980
Sodium carbonate	—	316
Sodium phosphate, dibasic	—	188
Sodium phosphate, monobasic	140	—
Sodium acetate	50	—
Sodium citrate	—	7
Sodium chloride	6,600	6,140
Calcium chloride	200	204
Potassium chloride	400	—
Potassium phosphate, monobasic	—	8
Potassium iodide	—	0.3
Magnesium sulfate · $7H_2O$	200	124
Manganous sulfate · H_2O	—	1
Cupric sulfate · $5H_2O$	—	1
Ferrous sulfate · $7H_2O$	—	2.5
Ferric nitrate	2	—
Zinc chloride	—	0.04
Sodium	3,305	3,587
Potassium	208	201
Calcium	72	74
Magnesium	20	12
Chloride	4,346	3,875
Phosphate	110	132
Carbonate	—	292
Bicarbonate	1,515	2,050
Organic:		
Glucose	1,000	1,250
L-Arginine	70	80
DL-Alanine (L)*	50	37
Glycine	50	37
DL-Glutamic acid (L)*	150	105
L-Glutamine	100	4
L-Histidine	20	80
DL-Isoleucine	40	57
DL-Leucine (L)*	120	57
L-Lysine	70	80
L-Proline	30	46
L-Hydroxproline	10	77
DL-Phenylalanine (L)*	50	75
DL-Threonine (L)*	60	30
DL-Tryptophane (L)*	20	70
L-Tyrosine	40	91
DL-Serine (L)*	50	53
DL-Valine (L)*	50	38
DL-Aspartic acid (L)*	60	71
DL-Methionine (L)*	30	46
L-Cystine	20	—
L-Cysteine monohydrochloride	—	0.1
Ascorbic acid	0.05	376
Glutathione	0.05	—
Pyruvate, sodium	—	76
Lactic acid	—	(0.922 ml)
Creatine · H_2O	—	33
Succinic acid	—	4
DPN	—	2
TPN	—	2
Coenzyme A	—	2
Adenine	10.0	—
Guanine	0.3	—
Xanthine	0.3	—
Cholesterol	0.2	—
Hypoxanthine	0.3	—
Thymine	0.3	—
Uracil	0.3	—
Adenylic acid	0.2	—
Ribose	0.5	—
Desoxyribose	0.5	—
Tween 80	0.005	—
Bacto-phenol red	20	—
Adenosinetriphosphate	1.0	4
Nicotinamide	0.025	—
Pyridoxal	0.025	—
Vitamin A	0.10	—
Vitamin D	0.10	—
Vitamin K	0.01	—
Vitamin B_{12}	—	0.003
Choline chloride	0.50	100
Biotin	.01	0.1
P-aminobenzoic acid	.05	0.2
Folic acid	.01	0.1
Inositol	.05	0.1
Niacin	.025	1.0
Pantothenate, calcium	.01	1.0
Pyridoxine	0.025	1.2
Riboflavin	0.010	1.0
Thiamine	0.010	1.0
a-tocopherolphosphate (disodium)	0.010	1.2
CO_2	to pH 7.2	*

* Gasphase is 5% CO_2, 20% O_2, 75% N_2

sule. Originally the lenses were picked up with the epithelial surface against the loop and flipped in the culture tube so that the epithelial surface was in contact with the media.

This procedure resulted in circular, centrally placed irregular lesions of elongated pyknotic nuclei in the epithelium but apparently the glycolytic and mitotic activity of the lens was not affected during short-term cultures. However, the present procedure of transporting the lens with the posterior pole against the loop and slipping it off into the media has been used in almost all of the present experiments. The contralateral lens always served as a control and was fixed immediately in Carnoy's or was cultured under the experimental conditions noted in the tables. In general the data obtained under a given set of experimental conditions were accumulated from several series of cultures.

The physical plant is essentially that of

TABLE 2

MITOTIC ACTIVITY OF EPITHELIUM OF LENSES CULTURED IN UNSUPPLEMENTED TC199

No. of Lenses	Time (hr.)	Differential Count (%)			Total Number of Mitotic Cells/Epith.		Experimental/ Control
		Pro.	Meta.	Ana. and Telo.			
		Avg. ±S.D.	Avg. ±S.D.	Avg. ±S.D.	Avg.	(range)	Avg. ±S.D.
5	0	25 ± 3	52 ± 3	23 ± 4	137	(74–343)	
5	2	27 ±10	64 ±14	9 ± 7	42	(5–136)	0.25 ±0.04
3	0	21 ± 4	57 ± 3	22 ± 2	157	(56–243)	
3	3	13 ± 9	78 ±17	9 ± 8	147	(11–273)	0.74 ±0.39
11	0	18 ± 7	56 ± 7	27 ± 5	166	(115–326)	
11	4	13 ± 7	59 ± 8	28 ± 9	129	(30–358)	0.75 ±0.29
10	0	20 ± 7	54 ± 5	26 ± 4	199	(75–460)	
10	6	11 ± 6	64 ±13	25 ±13	165	(24–464)	0.75 ±0.22
4	0	26 ± 3	56 ± 3	18 ± 1	203	(185–273)	
4	8	27 ± 2	55 ± 3	18 ± 5	90	(31–169)	0.48 ±0.29

Merriam and Kinsey.[6] The culture medium used was TC199 (Difco) with 5.0 cc. of medium per lens. Table 1 sets forth the composition of TC199 and KEI No. 2, the latter medium being currently in use by Kinsey and Wachtl.[3,4] The special gas mixture used in their procedure was not available at the start of these experiments and the lenses were incubated with air as the gas phase. Since preliminary experiments were successful, this practice has been continued. An increase in buffering capacity of the media was provided by the addition of 9.0 to 34 percent of 1.2-percent hypertonic Tris (hydroxymethyl) aminomethane (Sigma 7-9),* pH 7.5 to 7.7, as indicated in the appropriate tables describing the results of experiments. All procedures were conducted under as sterile technique as possible and practical.

The media of individual tubes were plated on blood agar plates at the end of the experiment to check the possibility of contamination. The lenses were examined at the end of each culture for clarity or gross changes. Flat preparations of lens epithelium for mitotic cell counts were prepared by the method of Howard as modified by von Sallmann.[7] Mitotic cells in prophase to in telophase were counted. Recently divided cells were not counted. Very late prophases were counted as metaphases except in the colchicine studies where they were counted separately from the true "band" metaphases. The glucose (hexose) and lactic acid content of the medium before and after individual cultures were determined by color development with anthrone[8] and p-hydroxydiphenyl[9] respectively.

*pH measurements were made routinely at room temperature (25±2°C.). The temperature differential of Tris is −0.015 pH/°C. increase (Sigma 7.9, Bulletin 106, Sigma Co., St. Louis); that of TC199 is approximately −0.002.

EXPERIMENTAL AND RESULTS

The first experiments (table 2) in which unsupplemented TC199 was used showed that the epithelium of lenses cultured in this medium for two hours had a very low mitotic count (25 percent of control lenses). The differential count showed that the percent of mitotic cells which were in prophase was similar to that of in vivo lenses but there was an increase in metaphases and a marked decrease in telophases. After three to six hours the total number of mitotic cells found in the epithelium of cultured lenses was approximately 75 percent of that of the uncultured, contralateral lenses. The differential count of mitotic cells in these epithelia showed a decreased percentage of prophases

and an increased percentage of metaphases which suggested that the unsupplemented media was not maintaining normal mitotic activity during this culture period. A decline of mitoses to 48 percent of the controls occurred at eight hours. Examination of the media after culture indicated that the failure in the latter case was probably due to a decrease in pH as lactic acid accumulated.

To check this possibility 0.5 to 1.0 cc. of Sigma 7.9, 1.2 percent hypertonic, pH 7.52 or 7.7, was added to each experimental tube (table 3A). The supplementation of the media with buffer resulted in a marked increase in mitotic activity of the epithelium of these lenses in each case compared to that of the control, contralateral lenses cultured in unsupplemented media. The low mitotic cell count of the controls, which were also cultured, may have been due in part to the use of older animals[7] in these earlier experiments.

In view of the beneficial effect of additional buffer, the time series was repeated and extended to 24 hours. The buffer (17 percent, pH 7.5) was added directly to the media before incubation. These results are presented in Table 3B. Again a low mitotic cell count (42 percent of control lenses) at two hours was found. The differential count showed a concentration of prophases similar to that of control lenses, an increase in metaphases, and a marked decrease in telophases as observed in the previous two-hour cultures.

After 12 to 16 hours the number of mitoses in the epithelium of cultured lenses was similar (102 percent and 83 percent respectively) to that of in vivo controls (lenses fixed at zero time). The differential count

TABLE 3

THE EFFECT OF SUPPLEMENTATION OF TC199 WITH 9.0 TO 17-PERCENT TRIS BUFFER ON THE MITOTIC ACTIVITY OF EPITHELIA OF LENSES CULTURED FOR TWO TO 24 HOURS

	No. of Lenses	Time (hr.)	"Tris" Added	Differential Count (%)			Total Number of Mitotic Cells/Epith.		Experimental/ Control
				Pro.	Meta.	Ana. and Telo.			
			%, pH	Avg. ±S.D.	Avg. ±S.D.	Avg. ±S.D.	Avg.	(range)	Avg. ±S.D.
A.	3	6*	—	29±1	50± 1	21±2	85	(58–105)	
	3	6	9, 7.7	30±5	53± 6	17±0	140	(115–157)	1.75±0.22
	3	6*	—	38±9	45±15	17±7	42	(12– 70)	
	3	6	17, 7.5	21±2	58± 3	21±2	190	(181–197)	7.63±5.84
B.	4	0	—	25±9	52± 7	24±6	239	(174–284)	
	4	2	17, 7.5	26±5	67± 6	7±6	109	(6–174)	0.42±0.23
	5	0	—	23±2	51± 4	26±5	178	(20–279)	
	5	12	17, 7.5	23±2	50± 5	27±6	175	(24–326)	1.02±0.12
	3	0	—	22±2	59± 6	19±3	255	(235–265)	
	3	16	17, 7.5	28±4	51± 1	21±4	212	(186–225)	0.83±0.11
	2	16*	17, 7.5	27±1	52± 3	21±1	174	(151–196)	
	2	20–24	17, 7.5	22±7	47± 7	31±0	57	(52– 62)	0.33±0.01
C.	6	0	—	22±3	49± 6	29±5	255	(126–449)	
	6	16	17, 7.7	19±9	51±11	31±5	122	(51–202)	0.49±0.19
	3	0	—	14±7	56± 2	30±5	186	(96–270)	
	3	20	17, 7.7	13±2	56± 3	32±2	111	(49–157)	0.58±0.06
	4	16*	17, 7.7	11±3	63± 4	27±5	137	(97–228)	
	4	20–24	17, 7.7	12±5	67±10	22±9	78	(24–144)	0.56±0.29

* Control contralateral lenses also cultured.

TABLE 4

THE EFFECT OF SUPPLEMENTATION OF TC199 WITH 17 TO 34-PERCENT TRIS ON THE MITOTIC ACTIVITY OF EPITHELIA OF LENSES CULTURED FOR 12 TO 24 HOURS

	No. of Lenses	Time (hr.)	"Tris" Added	Differential Count (%)*		Total Number of Mitotic Cells/Epith.		Experimental/ Control
				Pro.	Meta.			
			%, pH	Avg. ±S.D.	Avg. ±S.D.	Avg.	(range)	Avg. ±S.D.
A.	4	12	17, 7.5	25±3	45± 5	173	(131–194)	
	4	12	29, 7.5	24±5	51±12	181	(128–218)	1.04±0.12
	1	12	17, 7.5	33	62	162		
	1	12	34, 7.5	28	46	72		0.44
B.	3	0	—	26±5	50± 5	419	(395–531)	
	3	16	29, 7.5	26±6	51± 5	396	(374–426)	0.98±0.16
	4	16	29, 7.5	22±5	52±11	180	(70–342)	
	4	20	29, 7.5	26±8	55± 2	184	(69–368)	0.98±0.11
	4	16	29, 7.5	31±4	47± 2	253	(121–423)	
	4	24	29, 7.5	26±5	50± 5	176	(120–235)	0.79±0.25
C.	3†	0	—	21±4	53± 4	193	(142–218)	
	3†	16	29, 7.5	12±9	46±11	78	(20–129)	0.43±0.23

* Percentage of mitotic cells which were in a stage later than metaphase is omitted from the table.
† Contaminated series.

at 12 hours was remarkably similar to that of in vivo lenses and was not significantly different from that of the controls at 16 hours.

A decrease in mitoses to 30 percent of controls was observed at 20 or 24 hours and the differential count data were suggestive of a failure of cells to enter mitosis. It was of interest to observe the excellent maintenance of mitotic activity at 12 hours despite the very wide range of total number of mitotic cells per epithelium (20 to 279).

Further study of the effect of pH of the media was made by using Tris buffer at pH 7.7 (table 3C). The use of this media with a slightly higher initial pH did not maintain the mitotic activity of lens epithelium for a longer period than media with an initial pH of 7.5. There appeared to be a detrimental effect of this higher pH buffer as the total mitotic count at 16 hours was 50 percent of in vivo lenses compared to 83 percent in the case of the pH 7.5 media. The mitotic activity of lenses cultured for 20 hours in the pH 7.7 media was approximately 58 percent of the control lenses. Although the differential counts of the mitoses of cultured lenses were more variable than that of in vivo lenses, they were not significantly different.

It became apparent from the foregoing data that the pH and the buffering capacity of the media were important in maintaining a normal mitotic activity of cultured lenses. The effect of diluting the media with increasing amounts of 1.2-percent hypertonic Tris, pH 7.5 was studied (table 4A). Increasing the level of buffer from 17 percent to 29 percent did not adversely affect the mitotic activity of lenses cultured for 12 hours. The reproducibility of these cultures was found to be very good. Increasing the buffer level to 34 percent was apparently detrimental, and the activity of the experimental lens declined to 44 percent of the control. The number of lenses involved was too small to be conclusive. Longer periods of culture (table 4B) showed that a level of 29-percent buffer maintained the mitotic activity of lenses approximately 98 percent of the contralateral eye for 20 hours. The reproducibility of these cultures was again shown by the maintenance of the differ-

ential count in the experimental lenses compared to that found in vivo or to the contralateral lens cultured for a shorter period despite a very high mitotic activity (395 to 531 cells) or a wide range of activity (70 to 342 cells).

During these studies the epithelia of lenses of a series of contaminated cultures were studied to determine its effect on mitoses (table 4C). The total number of mitotic cells was found to be 43 percent of the control. The differential count showed a decline in the percent of prophases suggestive of a failure of cells to enter mitoses.

The decline of mitoses at 16 to 24 hours was further explored on the basis that it might be due to the accumulation of waste products which acted as inhibitors or to the exhaustion of an essential nutrient. Consequently, the media containing 29-percent buffer was replaced at 16 hours with fresh media. The failure of this procedure (table 5) suggested that, since mitosis was already at the decline point, the affected process might not be reversible. The experiments were repeated and the media (17-percent buffer) was replaced at approximately 10 hours when the mitotic activity was normal. However, a very low mitotic cell count (20 to 30 percent of controls) was again obtained at 20 to 24 hours.

In considering the reasons for the low mitotic cell counts at the various culture periods, it seemed apparent that the low mitotic activity at two hours might be explained on the basis of undetermined factors related to the shock of removal of the lens from its natural environment. On the other hand, the recovery of mitoses at four hours suggested the requirement of a substance which might accumulate, such as lactic acid, or diffuse out from the lens, such as ascorbic acid.

Both of these substances are present in appreciable quantities in KEI No. 2 and aqueous but are essentially absent in TC199. However, the addition of 20 mg. percent of either of these compounds did not appear to have any beneficial effect. The inadvertent addition of twice that amount in each of two other cultures for several hours proved deleterious.

In view of the low count at two hours, and again after 16 hours, the possibility existed that the mitotic count represented an accumulation of mitoses which remained static for several hours and then completed the mitotic cycle (degenerated cells are seen very

TABLE 5

EFFECT OF REPLACEMENT OF MEDIA AT 16 OR 10 HOURS ON MITOTIC ACTIVITY OF LENSES CULTURED FOR 20 TO 30 HOURS

No. of Lenses	Time (hr.)	"Tris" Added	Differential* (%)		Total No. of Mitotic Cells		Experimental/ Control
			Pro.	Meta.			
		%, pH	Ave. ±S.D.	Ave. ±S.D.	Ave.	(range)	Ave. ±S.D.
Media renewed at 16 hours							
2	16	29, 7.5	21 ± 1	51 ± 1	174	(82–265)	
2	24	29, 7.5	25 ± 9	42 ± 1	102	(100–104)	0.83 ±0.46
2	16	29, 7.5	21 ± 8	56 ± 4	343	(311–374)	
2	30	29, 7.5	27 ± 3	47 ± 1	47	(27– 67)	0.14 ±0.05
Media renewed at 10 hours							
3	0	—	35 ± 5	40 ± 8	232	(111–344)	
3	20	17, 7.5	36 ±12	32 ±11	78	(33–142)	0.32 ±0.07
2	0	—	35 ± 6	41 ± 6	113	(97–229)	
2	24	17, 7.5	23 ±23	52 ±20	33	(25– 41)	0.22 ±0.04

* Anaphase and telophase percentage omitted.

infrequently in the germinative zone of epithelia of cultured lenses). This explanation did not seem valid as there was excellent agreement in the successful periods of four to 12 hours between the differential and total mitotic counts of uncultured lenses and those of cultured contralateral lenses with mitotic counts varying from 22 to 600. However, the differential count of lenses cultured for two hours was not normal and that of lenses cultured for longer periods frequently showed a decrease in percent of prophases.

The mitotic activity was therefore checked by the use of a mitotic inhibitor, colchicine, which inhibits mitosis at metaphase. The interesting result was obtained (table 6A) that the low total mitotic count found in the epithelium of lenses cultured for two hours did not represent an inhibition of mitosis. There was an accumulation of some 150 metaphases in active epithelia and approximately one and one-half times the number expected for one two-hour cycle.

A possible explanation for this observation is that during the initial culture period, the time required for completion of a mitotic cycle is considerably shortened and fixation, at a given moment, catches only a portion of the cells during mitoses. The number of cells entering mitosis during a given time

TABLE 6

MITOTIC CYCLE OF LENSES CULTURED FOR TWO TO 24 HOURS AS DETERMINED BY THE USE OF COLCHICINE* ADDED TWO HOURS PRIOR TO TERMINATION OF CULTURE

	No. of Lenses	Time (hr.)	"Tris" Added	No. of mitotic cells/epithelium			No. Metaphases Expected or Found	Colchicine/Control
				Pro.	Pre-Meta	"Band" Meta		
			%, pH	Avg.	Avg.	Avg.	Avg.	Avg. ±S.D.
A.	1	0	—	44	11	31	86	1.46
	1	2	—	3	—	126	126	
	1	0	—	4	2	6	12	
	1	2	—	0	—	37	37	2.64
	3	0	—	46	20	71	137	
	3	2	17, 7.5	17	—	181	181	1.37±0.19
	4	2	17, 7.5	14	16	19	48	
	4	2	17, 7.5	4	—	150	150	4.09±1.87
B.	2	0	—	67	42	50	158	
	2	12	17, 7.5	2	—	190	190	1.20±0.03
	3	12	17, 7.5	69	49	115	232	
	3	12	17, 7.5	24	—	359	359	1.58±0.26
	6	0	—	38	32	65	135	
	6	16	17, 7.5	10	—	210	210	1.56±0.20
C.	4	0	—	69	26	102	197	
	4	20	17, 7.5	3	—	150	150	0.77±0.20
	3	—	—	37	23	105	165	
	3	24	17, 7.5	1	—	65	65	0.42±0.12
	2	16	29, 7.5	72	42	115	229	
	2	24	29, 7.5	4	—	151	151	0.67±0.04
D.	4	0	—	52	26	99	177	
	4†	16–24	17, 7.5	2	—	28	28	0.16±0.14

* Colchicine present at 2×10^{-5} M concentration.
† Contaminated cultures.

TABLE 7

THE EFFECT OF VARIOUS DRUGS IN VITRO ON MITOTIC ACTIVITY OF EPITHELIUM OF LENSES CULTURED FOR SIX TO 12 HOURS

No. of Lenses	Time (hr.)	Differential (%)		Total No. of Mitotic Cells/Epith.		Experimental/ Control
		Pro.	Meta.			
		Avg. ±S.D.	Avg. ±S.D.	Avg.	(range)	Avg. ±S.D.
Myleran*						
11—	8^3, 10^3, 12^5	25± 3	55±5	240	(84–491)	1.05±0.20
11 M	8^3, 10^3, 12^5	24± 5	55±6	253	(53–481)	
Chlorambucil*						
8—	8^4, 10^2, 12^2	23± 3	52±5	299	(160–663)	
8 C	8^4, 10^2, 12^2	19± 4	58±6	250	(133–614)	0.84±0.15
Alloxan†						
2—	10	27± 7	49±6	141	(130–152)	
2 A	10	21± 6	59±3	112	(108–117)	0.80±0.03
NaSCN‡						
5—	6^1, 8^2, 12^2	25± 8	53±7	196	(138–241)	
5 N	6^1, 8^2, 12^2	24±10	55±9	222	(149–267)	1.15±0.10
Diamox§						
6—	0	24± 3	54±5	252	(202–371)	
6 D	6–8	24± 4	58±5	136	(40–211)	0.57±0.25
4—	6	27± 3	50±7	141	(114–196)	
4 D	6	26± 2	50±6	154	(102–201)	1.10±0.04

* 0.2 cc. of a saturated solution in saline per culture tube (5 cc.); one-half of the series was in media supplemented with 17% "Tris" (1.2% hypertonic, pH 7.52); the remaining series were supplemented with 50–60 mg. Na_2HPO_4/100 cc. media.

† Alloxan = 7×10^{-6} M; media with 17% Tris, pH 7.52.

‡ NaSCN = 2×10^{-4} M conc.; media with 17% Tris, pH 7.5, or 84 mg. Na_2HPO_4/100 cc. media in one culture. This latter case (6 hours), control and exp'l, as well as a similar culture (tubes 7, 9, 10; table 8, exp. 1) showed the presence of 40–50% prophases in contrast to an average of 25% in most cultures.

§ Diamox = $2–4\times10^{-6}$ M; media without buffer in first series and with Tris in second series. The superscript in column "Time" refers to the number of lenses cultured for each time period.

period remains the same as in the control lenses.

The epithelia of lenses cultured for 12 to 16 hours (table 6B) also showed the presence of approximately one and one-half times the number of metaphases expected. The duration of the mitotic cycle in cultured lenses thus appears to be one to one and one-half hours. The accumulation of metaphases in epithelia of lenses cultured for 20 hours (table 6C) was approximately 80 percent of that expected and for 24 hours was 42 percent. The result obtained with several contaminated cultures (table 6D) in this series of experiments showed only 16 percent of expected number of metaphases in lenses cultured for 16 to 24 hours.

It can be concluded from the foregoing data that the mitotic activity of lenses can be routinely successfully maintained in buffered TC199 for a period of approximately 16 hours.

Preliminary use of the culture technique has been made to study the effect of various compounds on the mitotic activity of lenses in vitro (table 7). Myleran®,* which produces cataracts only when fed to rats and results in increased mitotic cell counts[5] in vivo, was without effect on rabbit lenses in vitro. Leukeran®,† which when combined with Myleran therapy simulates X-irradiation therapy and is used alone for treatment of leukemia, tended to decrease the mitotic count of lens epithelium but the significance of this effect cannot be determined at this time. Alloxan, which causes diabetes in rab-

* 1,4 dimethane sulfononoxy butane and †chlorambucil, p-(di-2-chlorethyl aminophenyl butyric acid supplied through the courtesy of the Burroughs Wellcome and Company.

TABLE 8

THE POSSIBLE INFLUENCE OF TEMPERATURE VARIATION ON MITOTIC ACTIVITY (6 HOUR CULTURES)

Tube No.*	*Experiment 1*† *Inefficient Stirring* Compound Added	Total No. of Mitotic Cells/Epith.	*Experiment 2*‡ *Inefficient Stirring* Compound Added	Total No. of Mitotic Cells/Epith.	*Experiment 3*§ *Efficient Stirring* Compound Added	Total No. of Mitotic Cells/Epith.
1	—	*4*	—	*13*	—	*217*
2	Myleran	64	Tetrazolium	0	Myleran	299
3	—	*27*	—	*84*	—	*?*
4	Myleran	76	Tetrazolium	0	Myleran	199
5	—	*85*	—	*241*	—	*196*
6	Chloram.	7	Methylene Bl.	0	Chloram.	194
7	—	*185*	—	*264*	—	*160*
8	Chloram.	61	Methylene Bl.	0	Chloram.	133
9	—	*229*	—	*366*	—	*138*
10	NaSCN	295	Methylene Bl.	0	NaSCN	149

* Heating element extends from approximately tube No. 5 to No. 10 at bottom of bath; stirrer positioned near tube No. 10; temperature at center was 36.2°C; change from position No. 1 to No. 10 was less than 0.5°C.
† Media with 84 mg. Na_2HPO_4/100 cc.
‡ Media unsupplemented.
§ Media with 17-percent Tris, pH 7.5.

bits, with cataractous changes apparent in some instances in less than one week, tended to reduce the mitotic count in eight hours. This series is too limited to be conclusive. Diamox®,* which would inhibit the carbonic anhydrase of the lens and which penetrates into the aqueous, was apparently without effect. Thiocyanate did not appear to have a significant effect on the lens culture. The good agreement between the total cell counts and the differential cell counts of the control and the negatively affected experimental cultures is indicative of the reproducibility of the culture technique during a 12-hour culture period.

Several instances of a possible influence of small changes in temperature of the water bath were noted during the course of these studies. On two occasions in the very preliminary studies the lens in the tube farthest away from the heater showed a tremendous increase in mitotic activity; in one instance 1,000 cells were found. The water bath temperature which was at 37°C. was reduced to 36.2°C. for all subsequent studies. In addition during the present experiments the stirrer was inadvertently moved slightly during cleaning of the water bath, and the results tabulated in Table 8, experiment 1, were obtained. Each successive control lens showed an increased mitotic activity as the tubes approached the position of the stirrer. A second experiment was deliberately run under identical conditions with very similar results. The stirrer was then positioned for maximum efficient stirring and this successive difference in mitotic activity was not found (experiment 3). Further study of the effect of temperature on mitotic activity of lens epithelium in vitro is contemplated.

* 2-acetylamino-1,3,4-thiadiazole-5-sulfonamide, supplied through the courtesy of Lederle Laboratories.

DISCUSSION

KEI media has been used successfully to culture lenses for 18 hours[4] and TC199 supplemented with Tris buffer has maintained lenses routinely successfully in the present studies for approximately 16 hours. A com-

parison of the composition of the two media (table 1) shows that some 30 substances are not necessary to maintain the lens for this time interval. It was of interest to observe that lenses cultured for 16 hours, and in some instances for 24 hours, in buffered TC199 maintained their clarity, normal glycolytic activity, and normal mitotic activity despite the very low concentration of ascorbic acid in the media (0.05 mg./liter).

It is presumed that, if the presence of an ascorbic-dehydro-ascorbic system is essential for maintaining a normal lens, as reported by Schwartz and Leinfelder,[10] the balance of other ingredients in TC199 must serve in part these functions. However, in the present studies only partial success was obtained in culturing lenses for 24 hours by replacing the media with fresh media at 10 or 16 hours. This failure may be due in part to a depletion by a "wash-out" phenomenon of substances normally present in the lens and essential for its metabolism.

TC199, in addition to being low in ascorbic acid, does not contain metabolic cofactors present in the KEI media. Determination of the concentration of these substances in lenses cultured under the conditions of the present experiments will be necessary to clarify this point.

The effect on mitotic activity of lens epithelium of diluting TC199 with various amounts of buffer is summarized in Figure 1. Unsupplemented TC199 maintained an approximately normal mitotic activity of most cultured lenses for a period of three to six hours, after which time the mitotic activity decreased. Diluting the media by 17 percent with Tris (hydroxymethyl) aminomethane, pH 7.5, resulted in normal activity of cultured lenses for approximately 16 hours. The use of 29 percent "Tris" increased the

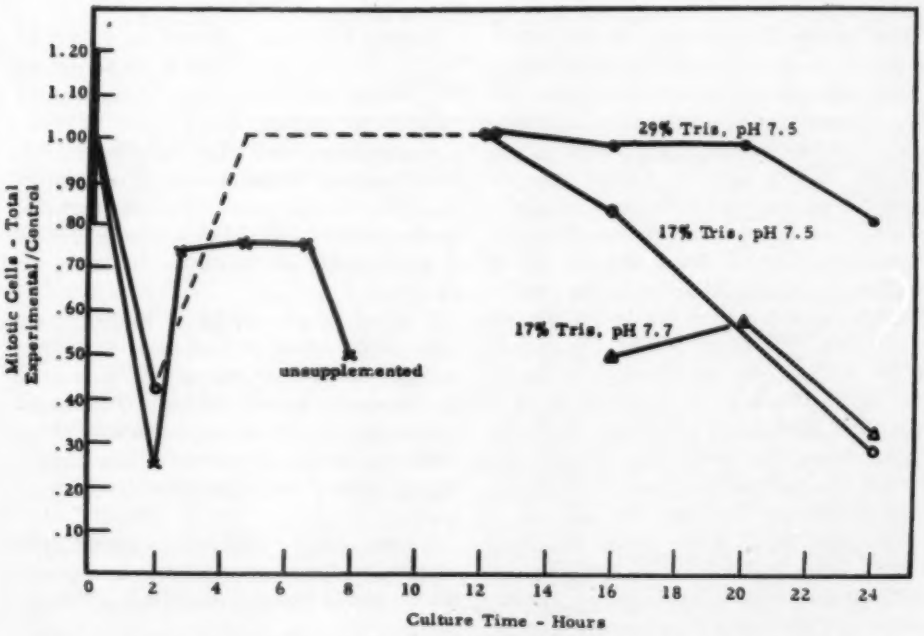

Fig. 1 (Constant). The maintenance of mitotic activity of epithelium of lenses cultured in TC199 supplemented with Tris buffer.

successful culture period to approximately 24 hours. The initial observation that 17 percent Tris at pH 7.7 did not maintain mitotic activity for 16 hours was puzzling. The experiment was repeated with similar results. An explanation for this failure is not apparent at the present time.

The initial pH of unsupplemented TC199 at 37°C. is 7.2. The initial pH of the supplemented media was 7.35 to 7.55 at 37°C. Numerous pH determinations after culture periods of 12 to 16 hours have shown that the pH of the media occasionally decreased 0.15 pH units but in most instances the decrease was 0.10 pH unit or less. In several determinations after 20-to 24-hour cultures, the pH decrease was no greater than after 16 hours. In contaminated cultures the pH decreased more than 0.20 pH unit. It would appear that normal mitotic activity of epithelium of lenses cultured in TC199 was maintained with a media pH of approximately 7.2 to 7.55.

One of the disadvantages of the culture technique is the essentially stagnant media which results in a depletion of nutrients and the accumulation of metabolites, especially lactic acid, which makes regulation of pH difficult. TC199 may be diluted approximately 30 percent with buffer and still maintain normal mitotic activity for 20 to 24 hours. Kinsey et al.[3] found that the use of additional sodium bicarbonate as buffer failed to support mitoses for 18 hours when lenses were cultured in TC199. The success of the present experiments may be due in part to the decrease in concentration of a substance detrimental to mitosis which occurred when the media was diluted with buffer. The successful culture for 16 hours with 17-percent Tris and the increase in culture time to 24 hours using 29-percent Tris indicate that additional buffering capacity of the media is also required. Further studies are necessary to determine whether supplementation with nutrients will permit a greater dilution of this media to increase its buffering capacity and still maintain the mitotic activity of lens epithelium.

The interesting observation was repeatedly made of an apparent decrease in mitotic activity of epithelium of lenses cultured for two hours. The inhibition of mitosis at metaphase by the use of colchicine showed that the mitotic activity of these lenses was normal. An explanation for this observation is that the period of the mitotic cycle was decreased. The use of colchicine indicated that the mitotic cycle of cultured lenses was approximately one to one and one-half hours. Colchicine, however, was not without effect on the mitotic activity of lens epithelium. In all instances the number of prophases present in these epithelia was considerably less than that found in the controls. Further study of this problem is contemplated using less toxic mitosis inhibitors.

Summary

Lenses have been cultured in TC199 at 36.2°C. for periods of two to 30 hours and the mitotic activity of the epithelium of these lenses studied.

Unsupplemented TC199 maintained a relatively normal mitotic activity of lens epithelium for only six hours. The failure of this media to maintain lenses for a longer period was apparently due to its low buffering capacity.

Diluting this media by 17 to 29 percent with 1.2-percent hypertonic Tris (hydroxymethyl) aminomethane, pH 7.5, resulted in the routinely successful maintenance of mitotic activity for 16 hours. In several experiments using 29-percent Tris, normal mitotic activity was maintained for 20 to 24 hours.

By the use of colchicine the mitotic cycle of cultured lenses was found to be approximately one to one and one-half hours' duration.

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IN VITRO EFFECTS OF SULFACETAMIDE*

On ocular strains of bacteria

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For the past 15 years, 30-percent sodium sulfacetamide has been used extensively in this country for the control of external ocular infections. In spite of the excellent clinical results with sulfacetamide,[1-3] there have been conflicting reports in the literature concerning the in vitro susceptibility of such organisms as Staphylococcus pyogenes to this drug. For example, Naimark and White[4] found that, by the use of a special liquid medium employing the test-tube method for sensitivity determinations, Staph. pyogenes was inhibited by a 30-percent concentration of sodium sulfacetamide. On the other hand, Shreck,[5] by the use of the disc and cup methods, found only 18 out of 200 strains of staphylococci susceptible to 30-percent sulfacetamide.

This study was an attempt to determine whether bacterial isolates from external ocular infections are sensitive to sulfacetamide in vitro and, if so, the quantitative levels of such sensitivity.

Methods and Materials

Ninety-one isolations of S. pyogenes and 10 isolations of gram-negative rods were made from cases of primary and secondary conjunctivitis by the following method:

Using aseptic techniques, cotton-swab cultures were taken from the lower cul-de-sac and placed immediately into thioglycollate liquid medium (without indicator). The tubes were incubated at 37°C. overnight. Microscopic studies, subcultures on blood agar plates, and biochemical tests (when indicated) were made for identification of the organisms. Only pure cultures were used

* From the Department of Ophthalmology, The Ohio State University.

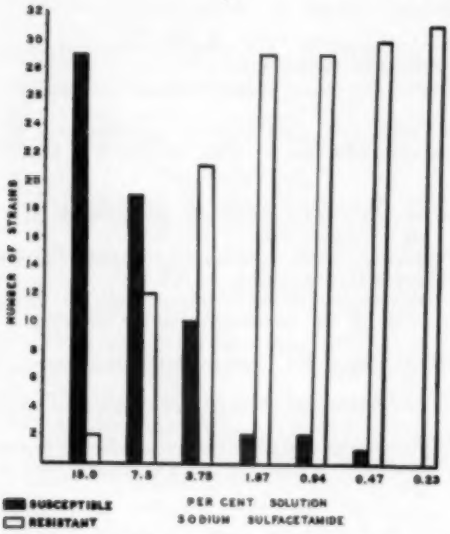

Fig. 1 (Leibold and Suie). Susceptibility of strains of coagulase-positive Staphylococcus pyogenes to sodium sulfacetamide (tube method).

for the sulfacetamide sensitivity determinations.

A loopful of culture from thioglycollate was subcultured into a fresh tube of thioglycollate and incubated at 37°C. for 20 hours. The following serial dilutions of 30-percent sulfacetamide were made using thioglycollate as the diluent: 1:2 (15 percent), 1:4 (7.5 percent), 1:8 (3.75 percent), 1:16 (1.8 percent) 1:32 (0.94 percent), 1:64 (0.47 percent), and 1:128 (0.23 percent). The final volume in each tube was 0.5 ml. One drop of a 1:50 diluted thioglycollate culture suspension was added to each of the above dilutions of sulfacetamide. Controls consisted of uninoculated thioglycollate without sulfacetamide and inoculated thioglycollate without sulfacetamide. All the tubes were incubated at 37°C. for 24 hours. After this period, growths within the tubes were graded as follows:

+++	Heavy growth (equivalent to controls containing organisms but no sulfacetamide)
++	Moderate growth
+	Light growth
0	No growth

Parallel studies of selected organisms were made using the disc method as follows:

Pour-plates containing the organisms in solid thioglycollate medium were made. Thirty-percent sulfacetamide-impregnated discs then were placed on the solidified medium. The petri dishes were incubated at 37°C. for 24 hours and then checked for zones of growth inhibition around the discs.

Findings

As may be seen in Figure 1 and Figure 2, practically all the ocular strains of Staphylococcus pyogenes were susceptible to 30-percent sodium sulfacetamide using the tube dilution method. Approximately 75 percent of these strains were inhibited by 7.5-percent solution of this drug. Only three strains out of a total of 91 were susceptible in the very high dilution of 0.47 percent. There was no appreciable difference of susceptibility between coagulase positive and coagulase negative staphylococci. Figures 3 and 4 show the degrees of inhibition which resulted from different concentrations of sulfacetamide.

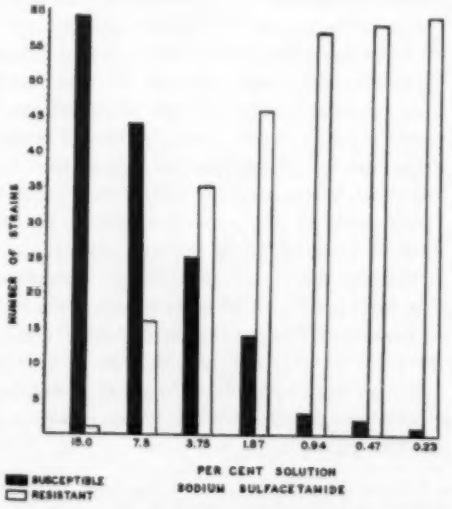

Fig. 2 (Leibold and Suie). Susceptibility of strains of coagulase-negative Staphylococcus pyogenes to sodium sulfacetamide (tube method).

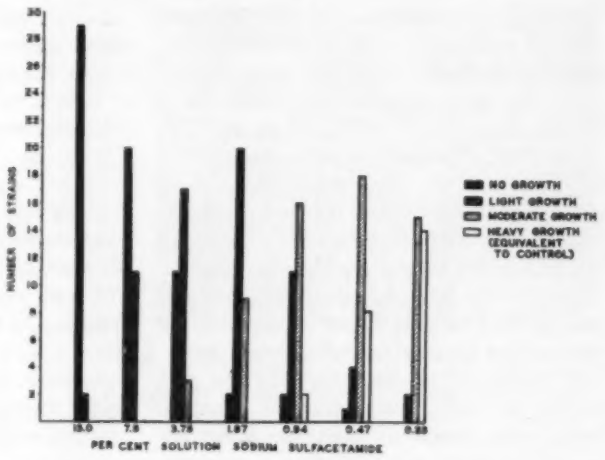

Fig. 3 (Leibold and Suie). Degrees of inhibition of strains of coagulase-positive Staphylococcus pyogenes to sodium sulfacetamide (tube method).

The results of the disc method for sensitivity determinations were disappointing since clear-cut zones of growth inhibition were not detectable against the staphylococci.

Sulfacetamide was effective in vitro against the few strains of gram-negative rods which were tested (table 1).

Discussion

As mentioned previously, this study was instigated primarily to determine the in vitro quantitative effectiveness of sulfacetamide against ocular strains of bacteria. The very few reports which have dealt with in vitro susceptibility of organisms to this drug do not appear to substantiate the excellent in vivo clinical and experimental[6] results. In

TABLE 1

IN VITRO EFFECT OF SULFACETAMIDE (TUBE DILUTION) ON GRAM-NEGATIVE RODS

Organism	No. of Strains	Average Level of Inhibition (percent sulfacetamide)
Pseudomonas aeruginosa	5	1.8
Proteus vulgaris	2	7.5
Chromobacterium sp.	1	.2
Aerobacter aerogenes	2	1.8

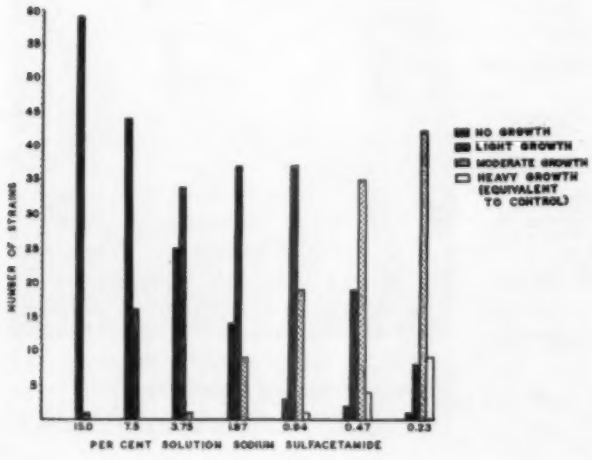

Fig. 4 (Leibold and Suie). Degrees of inhibition of strains of coagulase-negative Staphylococcus pyogenes to sodium sulfacetamide (tube method).

a total of 91 staphylococcal isolates from cases of conjunctivitis all except three were highly susceptible to 15-percent sulfacetamide. The most effective range of inhibition of these strains appeared to be from 7.5-percent to 15-percent sulfacetamide, although many of them were inhibited in much higher dilutions. This finding would tend to support the claims of the beneficial action obtained clinically with sulfacetamide.

This work has indicated also that the tube dilution method is far superior to the disc method for determining the staphylococcal sensitivity to sulfacetamide. In our hands, the disc method was not practical because the zones of inhibition were not sharply defined and, therefore, evaluation was difficult.

Sulfacetamide was an extremely effective agent against the few gram-negative bacilli tested. This is in accord with the findings of others.[7]

Conclusions

1. By use of the tube dilution method, sulfacetamide was effective in vitro against 88 out of 91 ocular strains of staphylococci.

2. The most effective range of inhibition appeared to lie between 7.5-percent and 15-percent sulfacetamide.

3. These findings tend to support the excellent clinical results with sulfacetamide in external ocular infections.

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EXENTERATION OF THE ORBIT*

With transplantation of the temporalis muscle

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The operation for exenteration of the orbit has usually been carried out by removing the orbital contents together with as much of the periosteum as possible allowing the denuded orbital surface to granulate or covering it with a Thiersch graft. When granulation is allowed postoperative dressings are necessary for from two to three months; when grafting is undertaken dressings are necessary for a minimum of six or more weeks. Both operations leave a deep unsightly orbital cavity which is most objectionable to patients. To date there has been possible no plastic repair to re-establish the orbit which could accommodate an acceptable prosthesis. Certainly any technique which lessens the mutilation of the usual types of orbital exenteration is desirable.

The temporalis muscle can be utilized to

* From the Institute of Ophthalmology of The Presbyterian Hospital.

fill partially the orbital cavity following an exenteration and for restoration of the socket which would make feasible the wearing of a prosthesis.

The temporalis muscle has been employed by plastic surgeons not only to supply dynamic force, such as for the correction of facial paralysis, but for the purpose of using its bulk and vascular qualities. Campbell[1] advocated the use of the temporalis muscle for repair and closure of traumatic lesions of the upper face as well as following monoblock excision of a neoplasm involving the bone of the upper face and orbit. Webster[2] used the temporalis muscle to repair large defects which resulted from the radical excision of a recurrent basal-cell epithelioma as well as for recurrent mixed tumor of the lacrimal gland. Naquin[3] was the first to advocate the use of the temporalis muscle to reduce the size of the orbital cavity following an exenteration. He transplanted the anterior one third of the muscle leaving the fascia.

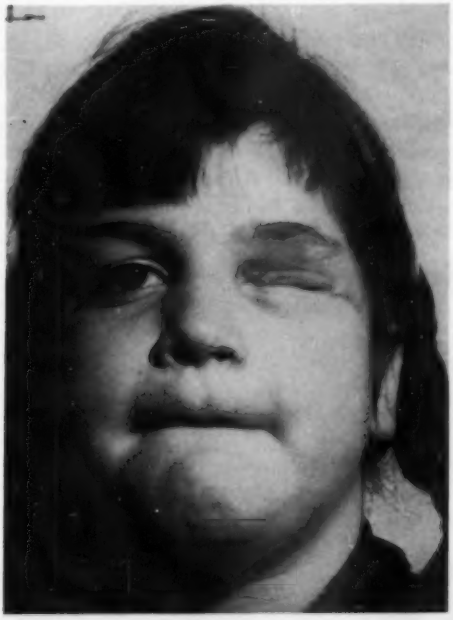

Fig. 1 (Reese). The appearance of a patient six months after an exenteration of the orbit with a temporalis muscle transplant. The patient had a rhabdomyosarcoma of the orbit.

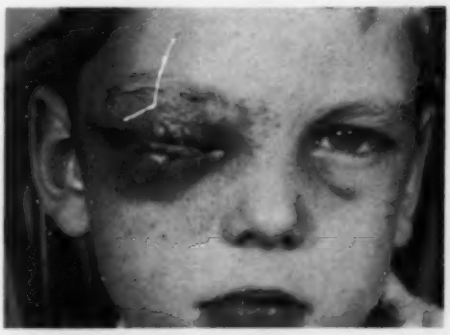

Fig. 2 (Reese). The appearance of a patient one week after exenteration of the orbit with a temporalis muscle transplant. The operation was done because of an embryonal myosarcoma of the orbit. No further dressings were necessary. (See fig. 7.)

A technique will be described here for transplanting the temporalis muscle together with its deep fascia following an exenteration. By combining the fascia with the muscle great bulk is furnished (fig. 6) to the transplant—a most desirable feature.

The individuals operated on, as well as the cadaver, indicate that the fascia is even thicker than the muscle. Contributing to this is a thick disc of cartilaginoid tissue in the central part of the fascia measuring approximately three cm. in diameter and almost one-cm. thick. This is appreciated particularly well in the cadaver dissection.

A considerable amount of the orbital space can be filled, and this leads to a cosmetic result which is much more acceptable to the patient (fig. 1). An additional advantage is the fact that no dressings are necessary one week to 10 days after the operation (fig. 2). Furthermore, the skin of the upper and lower lids with their cilia line can be retained, making possible a restoration of the orbit in which a prosthesis might be worn (fig. 7).

Criticism may be aimed at the procedure here described because the technique calls for the removal of only that portion of the periosteum which is in the quadrant in which

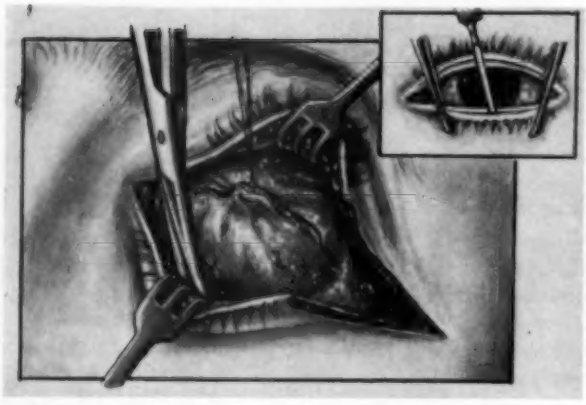

Fig. 3 (Reese). The upper and lower lids have been halved, leaving, anteriorly, the cilia and skin, and, posteriorly, the tarsus, orbicularis, conjunctiva, palpebral muscle, and fascial planes. The margins of the posterior half of the lid have been sutured together by a double-arm suture in the interest of easier manipulation when the exenteration is done. A horizontal incision extending from the external canthus temporally exposes the lateral bony wall and the temporal fossa. The insert shows the lid margin being halved by a scalpel. Two fixation forceps steady the lid.

the tumor existed. Some might fear that with transplanted tissue in the orbit a recurrence of a tumor might be masked and, therefore, not detected as early as it otherwise could be. I do not believe that these objections are serious deterring features. The operation leads to no difficulty with mastication. There may be no resulting depression in the temporal fossa, especially in children. In only one patient has this depression been a real blemish.

The technique of the operation is as follows:

The upper and lower lids are halved by an incision with a scapel through the gray line from one end of the lid to the other (fig. 3 insert). At the extremities of the lids this incision may be completed with scissors. This halving of the lids leaves, anteriorly, the cilia and skin, and, posteriorly, the tarsus, orbicularis, conjunctiva, palpebral muscle, and fascial planes. This division of the upper and lower lids is carried out to the orbital margin above and below (fig. 3).

A skin incision is made from the external canthus horizontally for from two to three centimeters. The dissection of this skin is continuous with that of the skin of the upper and lower lids and is carried out above and below to expose the entire region over the

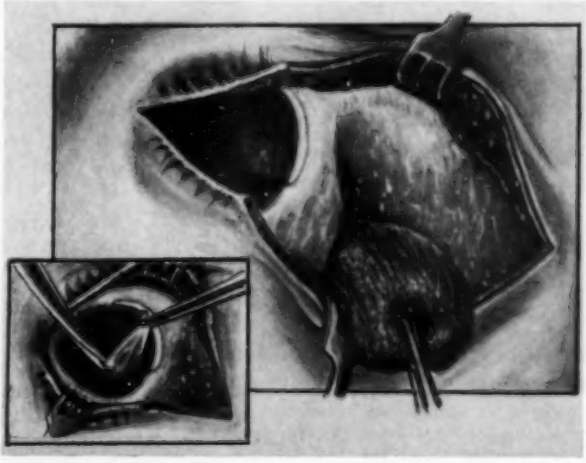

Fig. 4 (Reese). The orbit to the left has been exenterated. The temporal muscle and deep fascia have been mobilized from the temporal fossa. The insert shows the excision of the periosteum from the quadrant of the orbit which harbored the tumor.

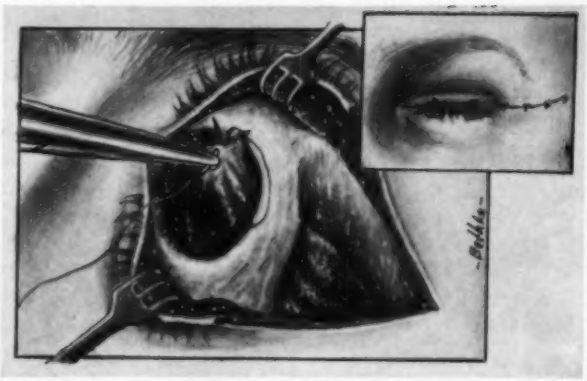

Fig. 5 (Reese). The temporalis muscle and deep fascia have been passed through the opening in the lateral wall of the orbit and are being sutured to the remaining periosteum. The insert shows the approximation of the lid margins with their cilia by two double-arm sutures and the horizontal incision is closed by interrupted catgut sutures.

temporalis muscle (fig. 3). When these upper and lower flaps, including the skin of the upper and lower lids and the skin of the temporal region, are now reflected, the entire orbital cavity is exposed together with a wide area in the temporal region.

The next step is to incise the orbital septum around the entire orbital circumference and to perform an exenteration, leaving the periosteum. After the orbital contents are removed, the periosteum from the quadrant of the orbit which harbored the tumor is removed by first making an incision in the periosteum at the orbital margin and reflecting the periosteum with an elevator and excising it (fig. 4 insert).

Next, an incision is made in the deep fascia along the origin of the temporalis muscle. The deep fascia with its underlying temporalis muscle is reflected from the temporal fossa (figs. 4 and 6). The fascia is incised from the upper margin of the zygomatic process where it is adherent.

The muscle is dissected down under the zygomatic process to its insertion into the coronoid process of the mandible. The muscle and fascia are freed until they are sufficiently mobile to reach the orbit easily. This dissection in the temporal fossa can usually be better accomplished if the bony shelf from the lateral wall of the orbit which overhangs the temporal fossa is ronguered (fig. 6).

With the Stryker saw a round opening is made in the lateral wall of the orbit. This is enlarged with ronguers, particularly below, but the anterior orbital margin is left. When the opening in the lateral wall of the orbit has been made sufficiently large, the temporalis muscle and its fascia are passed through the opening into the orbit and sutured to the remaining periosteum in such a way that the muscle and fascia are fanned out to fill uniformly as much of the orbit as possible (fig. 5). The lid margins are approximated with two double-arm catgut sutures (fig. 5 insert). A pressure dressing is applied. After

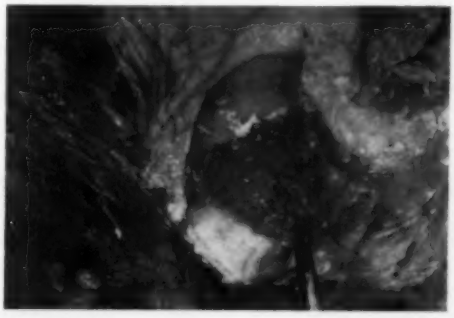

Fig. 6 (Reese). The temporalis muscle and its deep fascia dissected from the temporal fossa on a cadaver. The eye and orbital margin are on the right and the skin over the region of the temporal fossa has been dissected away and excised. Shown here is the great bulk furnished by the fascia of the muscle. The overhanging bony shelf from the lateral wall of the orbit is also seen. If this is ronguered a better exposure of the temporal fossa is afforded.

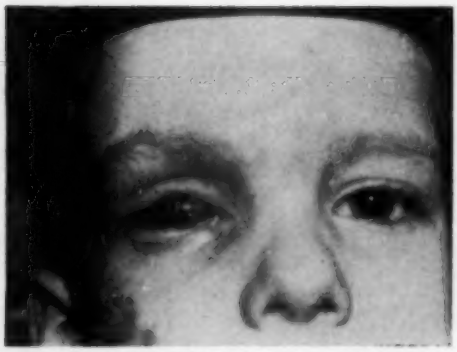

Fig. 7 (Reese). This is the same patient shown in Figure 2 seven months after exenteration of the orbit with temporalis muscle implant and one month after the restoration of the socket. The patient is shown here wearing a plastic conformer.

a week or 10 days no dressing is necessary.

Only when questioned about mastication do these patients say that during the early postoperative days they could not open their mouths as widely as usual. Later they have no complaints regarding mastication. When the mouth is opened during the act of chewing, there may be come retraction of the skin of the lid.

I propose to try to establish a socket so that the patient operated on can wear a prosthesis. To date I have attempted to restore the socket in only one patient after I felt that a suitable time had elapsed without evidence of a recurrence of the tumor. The patient on whom the restoration was attempted is shown in Figure 7.

The lid margins were severed between the two cilia lines and dissected far up above, below, and at the inner and outer canthus. A good cleavage plane was obtained between the lids and the transplanted tissue in the orbit which filled the cavity almost to its margin. From dental wax a stent was formed and covered with a Thiersch graft and inserted behind the lid into the prepared orbital space. The graft took well and a good cul-de-sac was obtained above, below, and at the inner and outer canthi.

Figure 7 shows the patient with a plastic conformer inserted into the restored socket. This conformer was later extruded and, because general anesthesia is necessary for any manipulation and insertion of a prosthesis, further efforts along this line have been deferred for the time being.

If there seems to be no contraindication, I plan in the future to restore the orbit at the time of the exenteration rather than as a secondary procedure. Since the essentials are present—to wit, the upper and lower lids with their cilia together with ample tissue in the orbit—there is no reason why an adequate socket for the prosthesis cannot be fashioned for these patients.

Five patients have undergone this type of exenteration.* Two of these were for rhabdomyosarcoma of the orbit; one for an embryonal myosarcoma; one for a malignant melanoma of the orbit which was an extension from a primary focus in the choroid; and one for a malignant melanoma of the conjunctiva.

73 East 71st Street (21).

* In a recent exenteration not included in this report a 20-mm. gold-ball implant was inserted into the apex of the orbit back of the temporalis muscle implant. This has been tolerated well and seems to be a worthwhile addition to the technique.

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OBSERVATIONS ON RETINOBLASTOMA*

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This study on retinoblastoma is based on 92 patients, 47 admitted to Childrens Hospital in Los Angeles, and 45 elsewhere. Microscopic examination of the involved eyes was carried out in 82 patients and the diagnosis of retinoblastoma was confirmed in 72, some other condition being found in the remainder. The 10 cases without microscopic examination were all admitted to Childrens Hospital for further retinoblastoma work-up and/or supportive measures. Three patients were in the terminal stage; another three were scheduled for enucleation but the parents refused; in four, enucleation was not recommended, as further follow-up and study failed to bear out the tentative diagnosis.

Information in the 47 patients admitted to Childrens Hospital was obtained by pediatric interns and residents in conjunction with the attending eye staff; whereas, in the 45, almost solely by ophthalmologists. In both groups, additional information was obtained from outside ophthalmologists and personal communications with the patient's parents whenever possible.

The majority of surgically removed eyes were submitted to Estelle Doheny Eye Foundation laboratory for gross and microscopic examination. All slides available there and at Childrens Hospital were re-examined microscopically not only to confirm diagnosis but also to insure uniformity of interpretation.

CLINICAL DATA

In this study, 72 patients were proved by microscopic examination to have retinoblastoma. There were more males (38) than females (34). In 22 cases, 12 of which were in males, both eyes were eventually involved, the left eye being first in 13 cases.

Chief complaints, noted in all except four cases, were:

Strange pupillary color or reflex	42
Muscle imbalance	19
Esotropia	5
Exotropia	8
Unclassified	6
Impairment of vision	11
Proptosis	5
Evidence of pain, irritability, etc.	4
Inflamed eye	4
Iritis	1
Difference in size of:	
Pupils	2
Corneas	1
Color of irises	1
Photophobia	1
Steamy cornea	1
Convulsions	1

Where more than one complaint had been listed, the most common pairs were:

Peculiar pupillary reflex and eye deviation (The latter usually comes first.)	8
Eye deviation and visual difficulty	6
Peculiar pupillary reflex and visual difficulty	3

In one instance, three complaints were listed: eye deviation, visual difficulty, and peculiar pupillary reflex. Visual difficulty was noted only when both eyes were involved, either simultaneously or one after the other.

One patient, brought in for routine eye examination because of prevalence of muscle imbalance in the family, was found to have retinoblastoma. One patient would not have seen a doctor had it not been for injury in the left eye. The admission of another patient with history of trauma was suggested because of intraorbital calcification discovered in the routine X-ray films.

Of the seven cases where symptoms were noted since birth, the complaints given were:

Peculiar pupillary reflex since birth	4
Eye deviation since birth	2
"Cancer" in the eye since birth	1

* From the Department of Ophthalmology, Los Angeles Childrens Hospital, University of Southern California School of Medicine, and The Estelle Doheny Eye Foundation.

The latest appearance of symptoms in this series occurred at six years of age. The youngest patient to undergo enucleation was aged two months, the parents having noted a peculiar "glare" in the child's eye two weeks prior to admission. In this case, the tumor could have been present since birth. The mean age at onset of symptoms was 17.1 months, and the mean age of initial enucleation, 23.2 months.

Family history was recorded in 32 cases. In one case, the child's father's aunt had four children, two of whom had retinoblastoma. In another case, the patients' grandmother when a child had "retinoblastoma" but enucleation was refused. In two other cases cancer (not specified) was mentioned on both sides of the family. Twenty-eight patients had completely negative family histories.

Satisfactory view of the fundus and localization of the tumor mass were obtained in only 39 cases, as the rest had hazy media—cloudy cornea, opaque lens, floater-studded vitreous. Usually the tumor mass had a pinkish-cream, fleshy appearance, and was well vascularized. Occasionally, flecks of calcium were detected by ophthalmoscopy. Schepen's scope was used sparingly. Of the 19 cases investigated by orbital X-ray films, seven proved positive. Transillumination was performed in 17 cases, 10 of which did not transilluminate well, a solid or darkish mass being seen. Isotope uptake studies were done in one case in which the uptake was found to be elevated 82 percent in the involved eye.

Intraocular pressure was taken with a tonometer and recorded in only a few of the cases. In several instances, only tactile tension was noted. Slitlamp examination was performed in a few cases, although all that was suggestive of its having been done was a note like, "flare, one plus," "cells, two plus," and so forth.

Enucleation was performed in all unilateral cases except in one moribund patient, where the diagnosis of retinoblastoma was confirmed only at autopsy. Nine out of 50 patients died. Not all the eyeballs had satisfactorily measurable optic-nerve stumps, due to faulty operative technique. In the 33 eyeballs where the optic-nerve stumps were measured, the average length was 5.5 mm. In three, the nerve was cut flush and in one it measured 23.3 mm.* Deep X-ray therapy was used in six unilateral cases following enucleation because of the pathologist's report of possible extrabulbar extension. In spite of this, four patients died.

TABLE 1

AGE AT ONSET OF SYMPTOMS AND MORTALITY (60 CASES)

Age at Onset of Symptoms	Patient's Status			
	Living	Deceased	Unknown	Total
Birth	2	4	1	7
2 wk.–3 mo.	6	2	0	8
Over 3 mo.–6 mo.	6	2	0	8
Over 6 mo.–12 mo.	5	3	0	8
Over 12 mo.–24 mo.	8	3	2	13
Over 24 mo.–36 mo.	4	3	0	7
Over 36 mo.–72 mo.	7	2	0	9
Further regrouping of cases as to age at onset shows:				
Birth—1 yr.	19	11	1	31
Over 1 yr.–6 yr.	19	8	2	29

Of the bilateral cases, nothing but unilateral enucleation was done in four patients, all of whom died. Unilateral enucleation, combined with deep X-ray therapy to the other eye, was carried out in nine cases, resulting in "cure" in four. In two of the five that died, X-ray therapy seemed to be helpful for about two months only.

Following is a brief summary of the cases "cured" by deep X-ray therapy:

CASE REPORTS

CASE 1

Seven-year-old Negro boy. The left eyeball was enucleated in July, 1950. X-ray therapy to right eye was started the following month. A tiny cicatrix marks the original site of the tumor.

CASE 2

Four-year-old white boy. The right eyeball was enucleated in May, 1952. X-ray therapy to left eye was started soon after. Cataract developed but

* Autopsy specimen.

this was later extracted. Vision 20/100+ with aphakic correction.

CASE 3

A two-and-a-half-year-old white boy. The left eyeball was removed in January, 1954. The right eye treated with X rays and the tumor flattened considerably. The child is currently healthy.

CASE 4

Three-and-a-half-year-old white boy. The left eyeball was enucleated when he was five months old. X-ray therapy in the right eye proved successful. However, there had been no recent follow-up.

In two of the seven cases in which bilateral enucleation was done, X-ray therapy was tried on the second eye but was discontinued in favor of enucleation. All except one patient are alive and in good health. In this lone fatal case, the time interval between the enucleation of the two eyes was 14 days. In the first eye, the tumor cells were confined to the globe but were within the sclera and beyond the lamina cribrosa in the second eye. The time intervals between enucleation of the two eyes in the surviving six patients ranged from five days to 13 months.

In one case, X-ray therapy was used on the other eye after enucleation of the first eye but failed. Nitrogen mustard, however, saved the eye. Only supportive measures were done in one patient admitted in the terminal stage.

Four cases, three of which were bilateral, underwent exenteration of the orbit but all died. In one of these, the procedure could not be completed because of extensive bleeding and the poor surgical condition of the patient.

An intracranial approach with complete excision of the involved optic nerve was done on a six-year-old girl, the oldest child in this series, eight days after enucleation or two days after exenteration of the orbit. This was resorted to because of the pathologist's report that there were tumor cells beyond the lamina cribrosa. For about a year the patient was doing well; however, following a three-month period of severe pain along the lower vertebral column, she succumbed to the disease. Autopsy examination revealed both intracranial and intraspinal metastases.

Of the 72 patients (fig. 1) in which the diagnosis of retinoblastoma was confirmed, 47 are known to be alive and in good health, 20 have died, and five could not be contacted. Excluding the cases without follow-up for statistical purposes, the case fatality rate would be 30 percent. Of the 50 unilateral cases, 37 patients are known to be alive, nine have died, and four have not been contacted, giving a case fatality rate of 20 percent. Of the 22 bilateral cases, 11 patients have died, 10 are in good condition, and one has no

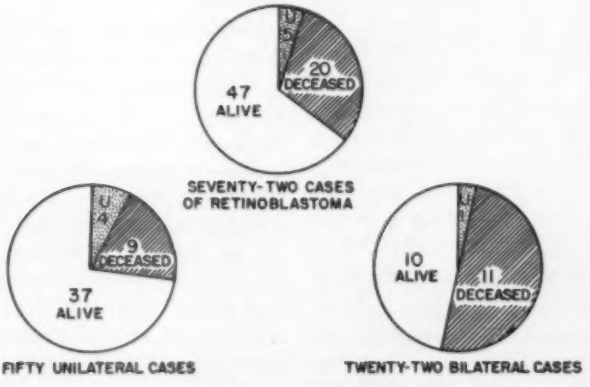

Fig. 1 (Carbajal). Case fatality in retinoblastoma. (*U* stands for the unknown or those cases with incomplete follow-up.)

follow-up, giving a case fatality rate of 54 percent.

The onset of symptoms was known in 60 of the 72 cases, and, as noted in Table 1, the case fatality rate was higher in those in whom the symptoms were noted at birth than when the symptoms were noted later. On further analysis, however, it appears that the age of onset does not have any direct relationship to the fatality of the disease. In the 31 cases where the age of onset ranged from birth to one year, 19 are living, 11 have died, and one is lost to follow-up. In the 29 patients in whom the age of onset ranged from over one year to six years, 19 are living, eight have died, and two unknown. As will be pointed out later, the duration of symptoms appears to bear some direct relationship to the case fatality. It may be assumed that, when the symptoms are noted at birth, the chances of putting off intervention are greater; hence, the higher fatality. In the seven cases in which the disease was evident at birth, the average duration of symptoms was 18 months.

It is evident from Table 2 that the case fatality rate was less when the duration of symptoms before initial treatment (enucleation chiefly) was two weeks to six months than when duration was more prolonged.

Following are the periods of survival after enucleation of the first eye of those who died:

Months of survival	No. of cases
0-3	1
4-6	1
7-12	8
13-18	1
19-24	2
25-30	3
31-35	1
36-40	1
41-50	1

Fifteen of the 47 survivors were followed five years or more, 13 were followed 36 to 59 months, 15 were followed slightly less than three years on the average, and five had inadequate follow-up. Excluding the five, the average time of follow-up was approximately 50 months.

TABLE 2

Duration of symptoms before initial treatment and mortality

Duration of Symptoms	Patient's Status			
	Living	Deceased	Unknown	Total
1 mo. or less	15	5	0	20
Over 1 mo.–6 mo.	14	4	2	20
Over 6 mo.–12 mo.	9	7	1	17
Over 12 mo. (25–30)	0	3	0	3

Diagnostic difficulties

Because of the extreme importance of early diagnosis of retinoblastoma, the 47 patients admitted to Childrens Hospital between 1933 and 1956, inclusive, all with the tentative diagnosis of retinoblastoma, are analyzed separately.

When funduscopic examination was unsatisfactory in the eye clinic because of non-co-operation or some haziness in the media, the child was usually examined under anesthesia. X-ray pictures for calcification of the orbit were taken in 25 cases, transillumination was done in six, isotope studies in three, and Papanicolau staining of the aqueous in two. It is noteworthy that only 27 of these patients had microscopic evidence of retinoblastoma, 10 having some other pathologic condition.

Enucleation was not performed in 10, three of whom were in the terminal stage of the disease. In another three, enucleation was urged by the eye staff but could not be performed because of the parents' refusal. In the remaining four, enucleation was not advised as there was not enough basis for a diagnosis of retinoblastoma on further follow-up studies. There were no intraorbital calcifications, what appeared to be an intraocular mass transmitted light well, tension was not elevated, and subsequent examinations revealed no significant change. In one particular case, both isotope study and

Papanicolau staining of the aqueous proved negative, and the patient during her last visit at the eye clinic was thought to have a congenital defect around the nervehead rather than a retinoblastoma.

In short, 27 out of 36 patients who underwent enucleation or biopsy of orbital tissue had retinoblastoma. At first glance, this may appear to be low diagnostic marksmanship. On further analysis, however, this rating of approximately 75 percent is satisfactory; it is better to err on the safe side. Two of the 10 eyes not enucleated later proved to have very malignant types of new growth. Final microscopic diagnosis in the 10 eyes supposed to harbor retinoblastoma showed:

Case	Condition
1	Detached retina
2	Acute retinitis with hemorrhage; massive exudate of posterior chamber and detached retina
3	Exudative retinopathy (Coats' disease)
4	Glaucoma
5	Retrolental fibroplasia; possible Coats' disease
6	Coats' disease
7	Malignant angio-endothelioma
8	Angioblastoma
9	Traumatic retinal hemorrhage
10	Possible intraocular fungus infection; detached retina

This may be broken down into:

Detached retina	3
Coats' disease	3
Malignant new growth	2
Inflammatory condition	1
Glaucoma	1
Retrolental fibroplasia	1
Retinal hemorrhage	1

In these 10 cases, the main misleading factors were (1) white reflex in the pupillary area noted by the parents and examining ophthalmologist, (2) pupil fixed to light, (3) muscle imbalance, (4) poor visibility of the fundus, and (5) tumor mass or the suggestion of it.

Pathology data

For the sake of simplicity, each of the eyeballs in this series was treated as a single sphere, the curvature of the cornea being ignored. The following formula[1] was used in the calculations:

Vol. of sphere = area of surface times one-third radius
Vol. of sphere = 0.5326 d^3 (approximate), where d stands for diameter

Using the preceding formula, the volume of the adult human eyeball according to dimensions cited by various authors is as follows, the average being seven cc.:

Merkell and Kallin[2] ..... 6.9 cc. (24.3 × 23.6 × 23.3 mm.)
Berens[3] ..... 7.1 cc. (24.15 × 24.3 × 23.48 mm.)
May[4] ..... 7.2 cc. (24 × 24.5 × 23.5 mm.)
Duke-Elder[5] ..... 6.8 cc. (24.15 × 24.13 × 23.48 mm.)
Wolff[6] ..... 6.7 cc. (24 × 23.5 × 23 mm.)

Actually, the volume of the normal adult eye is 6.5 cc.[3] when the curvature of the cornea is taken into consideration. It may then be concluded that, when an eyeball is treated as a simple sphere, it averages 0.5 cc. larger than the actual eyeball.

Two other considerations are:

1. The dimensions of the male eyeball are 0.5 mm. greater than those of the female.[7] In other words, the volume of the male is greater by 0.2 to 0.6 cc., depending on the age of the patient.

2. According to Duke-Elder,[5] the eyeball of the newborn is more spherical than that of an adult, although Doggart[8] states that at birth the vertical diameter of the eyeball is 14 to 15 mm. and the anteroposterior and horizontal diameters are 17 mm.

In this series, the dimensions* (anteroposterior, horizontal, and vertical diameters) of 53 eyeballs were taken with a caliper. Four others were simply described as small,

* In the calculation for the volume of the eyeball, the thickness of its three coats was entirely ignored. Also, the three diameters were added and then divided by three to arrive at the value of d in the formula.

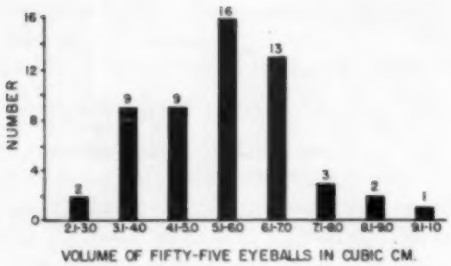

Fig. 2 (Carbajal). Distribution of eyeball volumes in retinoblastoma.

normal, or oversized. Some shrinkage may be expected, depending on the type of fixative* used and perhaps the time interval between enucleation and measurement of the eyeball.

The smallest eyeball, that of the youngest patient in this series to undergo enucleation, had a simplified volume of 3.05 cc., while the largest, that of a three-year-old Mexican boy in whom the tumor mass was mostly extrabulbar, measured approximately 23.6 cc. Also, I calculated the volumes of the eyeballs, using the two diameters measurable on the slides (celloidin sections), and found very slight shrinkage, ranging from 0.1 to 1.0 cc. If the four eyeballs that were not measured with calipers but the volumes of which have been calculated from the slide measurements are included, the smallest eyeball would measure 2.14 cc. Excluding this smallest eyeball and the one which measured 23.6 cc., the mean volume of the eyeballs (fig. 2) in this series is 5.8 cc. This indicates that an eye harboring a retinoblastoma tends to be normal in size, in contrast to an eye with retrolental fibroplasia, which tends to be smaller than normal, and one with congenital glaucoma where the eye attains monstrous proportions. Phthisis bulbi was noted only in one shrunken and deformed eyeball which measured 2.35 cc.

In only 18 eyeballs in this study were the corneal diameters recorded. According to both Berens[5] and Wolff,[6] the normal adult cornea measures 11 mm. by 12 mm. It is interesting to note that of all the structures of the eye, the cornea appears to assume a normal diameter not long after birth[8] and changes little except when the intraocular pressure is increased. In these 18 cases, the corneal diameters averaged 11 by 12.2 mm. (slightly above normal), while the volumes averaged 5.35 cc. The higher than normal average was due to three cases with far-advanced retinoblastoma. All of these patients died. Their eyeballs measured 11 by 13 mm., 13 by 14 mm., and 15 by 16.5 mm., giving an average of 13 by 14.5 mm. All three patients, aged seven, 10, and 15 months, respectively, had secondary glaucoma, proved both clinically and histopathological'y.

Another procedure routinely done on all the eyeballs received at the Estelle Doheny Eye Foundation laboratory is transillumination.† Fifty-four of the 57 eyeballs so examined proved positive, that is, something impeded the passage of light through the pupil, or a darkish mass was demonstrable. Since, according to Reese,[10] eyes containing retinoblastomas transilluminate fairly well unless a great portion of the tumor consists of calcium, it is possible that certain changes, like coagulation of vitreous or transudate, occur in the eyeball after its enucleation. However in the 16 cases in which transillumination was performed before enucleation, nine proved positive.

Calcium specks or flecks were seen grossly in the cut specimen in many of the cases. As will be mentioned later, calcification of varying degree, was noted microscopically in all of the cases except one. Since this is the feature pathognomic of retinoblastoma,[10] it is unfortunate that in the funduscopic findings in this series, the presence or ab-

* In the Estelle Doheny Eye Foundation laboratory, Zenker's and formalin are used as fixatives. No significant difference in shrinkage between the two has been found.[9]

† An American Optical microscope lamp with detachable glass cover and adjustible diaphragm was used.

sence of calcium foci was recorded only sporadically. In fact, X-ray pictures of the orbit were taken in only 19 of the 72 cases; seven of the films proved positive.

The tumor mass appeared to occupy the entire vitreous cavity in seven patients, five of whom died; over half of the vitreous cavity in 24, seven dying; and less than half of the vitreous cavity in 27, three dying. At first glance, it would appear as if fatality were directly related to the size of the tumor mass; however, it was not so much the size of the tumor as involvement of the optic nerve, the emissary veins, and the choroid; almost all of the fatal cases showed such findings. In each of two cases, an extremely large extrabulbar mass was present. Both patients died. Except in three cases, all available specimens showed tendency to an endophytum type of growth (toward the vitreous cavity). In one case, both endophytum and exophytum types of growth were demonstrable; and in two cases, both patients dying, the growth was entirely exophytum.

Contrary to the claims of Cummings and Sorsby,[11] there was no significant histologic difference between unilateral and bilateral retinoblastoma.

Daughter seedlings or implantation growths were seen in the majority of the cases. When there was no retinal detachment, the seedlings were usually confined to the retinal surface and, sometimes, the vitreous. Less frequent sites were the choroidal surface, ciliary epithelium, behind the lens, anterior chamber angle, and even the corneal endothelium. When retinal detachment was present, most of the daughter seedlings were seen in the subretinal space on the pigment epithelium or closely hugging the choroidal surface.

In a case that showed the picture of iritis clinically, implantation foci were deposited on the iris, lens capsule, and on the corneal endothelium, simulating mutton-fat keratic precipitates. In four other cases, tumor cells were found in the anterior chamber, on the iris, and on the corneal endothelium. In one of these, the angle had a sprinkling of tumor cells.

Two of these patients died from the disease, the fate of one is not known; while two patients, including one who appeared to have a full-blown iritis and who was heavily treated with antibiotics, are known to be alive and in good health.

Although retinoblastoma is well vascularized, there was only one case in this series in which definite intraocular hemorrhage was seen. The most common complication was glaucoma and 21 cases showed peripheral anterior synechias* of varying degree. Retinal detachment was evident in 15 cases, but did not seem directly related to the size of the tumor mass. In fact, it was more frequently seen in eyeballs harboring growths of smaller size.

Another late finding associated with retinoblastoma was cataract formation. Eleven cases definitely showed lens opacities. Corneal changes, which were seen in eight cases, consisted chiefly of epithelial edema. The stroma was vascularized in one case, and keratic precipitates consisting of tumor cells were seen in five. Bullous keratopathy was recorded in only one instance.

As previously mentioned there was just one case of phthisis bulbi, although another eye† was approaching this state. One case of hemorrhagic detachment of the choroid was observed. Ectropion uveae was demonstrable in only one case but there was no evidence of central vein obstruction by tumor cells.

The amount of calcification and necrosis in all cases examined seemed about equal. Both conditions were graded arbitrarily as absent, slight, moderate, or marked. How-

* Clinically, the number of cases with apparent secondary glaucoma was less because tonometry was not routinely done, tactile tension being relied upon mostly. In one case showing all the earmarks of an acute glaucoma, trephining surgery was performed.

† Reese, who was consulted regarding this, thought there was spontaneous regression of the tumor.

TABLE 3

RELATIONSHIP BETWEEN ROSETTE FORMATION AND MORTALITY

Type and Amount of Rosettes	Patient's Status			
	Living	Deceased	Unknown	Total
True Rosettes				
Practically absent	5	11	3	19
Slight	17	2	1	20
Moderate	11	1	1	13
Marked	6	0	1	7
Pseudorosettes				
Practically absent	2	5	2	9
Slight	12	4	3	19
Moderate	20	4	1	25
Marked	5	1	0	6

ever, fatality did not seem related to the degree of either.

Vascularization of the new growth was likewise graded but did not influence fatality.

In this series, a special attempt was made to divide the cases: (1) as to the amount of true rosette formation; (2) as to the degree of pseudorosette formation.* In each case, as many slides as available were re-examined and the amount of true and false rosettes was determined. In most of the cases, both were found in varying proportions. Again, the rosette formation was graded as practically absent, slight, moderate, or marked, depending on the average trend as revealed in all slides available. As will be seen in Table 3, not one patient died when there was marked formation of true rosettes and only one of those with marked formation of pseudorosettes. Nineteen cases out of 59 showed practically no true rosettes, while only nine failed to show pseudorosettes. Of the former group, 11 (or 57 percent) died, while of the latter, five (or 55 percent).

*A true rosette consists of a ring of columnar cells arranged around a central circular lumen which presents a faint limiting membrane along the inner border of the cells, while a false rosette consists of a few cancer cells growing around a small vascular channel. Another type of pseudorosette is formed when a small group of tumor cells degenerate, leaving a clear space that contains cellular debris surrounded by a ring of viable cells.[9]

When there was slight or moderate formation of true rosettes, three patients (nine percent) died; in the other group, eight (18 percent). It is interesting to note that five cases showed practically no true rosettes or pseudorosettes but had marked necrosis and calcification. All of these five patients died. Further analysis revealed that in all five, both choroid and optic nerve were invaded by tumor cells. As pointed out by Herm and Heath,[12] the longer the tumors exist, the more undifferentiated they become. This appears to be more tenable than the theory that the cells were undifferentiated right from the onset of the disease.

In these five cases, the duration of the disease was longer than six months (25 months in one), except in a six-year old girl, the oldest child in this series, who was brought to the clinic primarily because of exotropia of 20 days' duration. During the first clinic visit, a peculiar eye reflex was discovered and a whitish mass was seen in the left eye. From such a history it was apparent that the disease had been present at least six months. If this is so, the conclusion that fatality is directly related to the duration of the disease rather than to age of onset would seem to be true. A corollary to this might be that the longer the tumor has been present in the eye, the less likely that it will be differentiated.

Extension into the choroid (table 4) was seen in 26 cases (36 percent), higher than the 25 percent cited by Reese.[10] The extension was graded as:

Grade I. Tumor cells were confined to the choriocapillaris, adjacent to the pigment epithelium.

TABLE 4

RELATIONSHIP BETWEEN CHOROIDAL INVOLVEMENT AND MORTALITY

Grade	Patient's Status			
	Living	Deceased	Unknown	Total
I	9	4	2	15
II	3	5	1	9
III	0	2	0	2

Grade II. Tumor cells had invaded the larger vessels of the choroid but did not occupy the entire choroidal thickness.

Grade III. The entire choroidal layers were involved with tumor cells.

In this grading the number of patches where the choroid was invaded by tumor cells was not taken into consideration, although it appeared that when the entire thickness was affected, more patches of choroidal involvement were evident. Eleven of the 26 patients with choroidal involvement died. The two patients classified in Group III died, in contrast to only half of those in Grade I.

Scleral involvement was seen in seven cases (approximately 10 percent); four of these patients died. However, all four had some tumor cells in both optic nerve and choroid.

The most important consideration in this study is that of invasion of the optic nerve by tumor cells (table 5.)

Although the optic nerve appeared to be involved in 41 (56 percent) of the 72 cases, the tumor cells had extended into the optic nerve beyond the lamina cribrosa in only 21 cases (29 percent). Fourteen (69 percent) of these patients died. Of the remaining seven, who are known to be alive, three are older than four years, while the rest, at the time of writing this paper, had survived an average of a little over 10 years. Since, when measured, the length of the optic nerve stump varied from one mm. to four mm., it is possible that one or two of these surviving seven may still succumb to the disease. On the other hand, one of these patients, who showed tumor cells right at the end of the cut nerve and whose parents were notified of the gravity of the situation, has survived almost seven years, and is still known to be alive and in good health. In this case, however, there was no choroidal or scleral involvement. It is possible that no tumor cells were left beyond the site where the nerve was severed.

TABLE 5

RELATIONSHIP BETWEEN NERVE INVOLVEMENT AND MORTALITY

Portion of Nerve Involved	Patient's Status			
	Living	Deceased	Unknown	Total
Anterior				
Optic cup	5	1	0	6
Anterior to lamina cribrosa	10	2	2	14
Posterior				
Nerve axis only	3	12	0	15
Vaginal sheaths only	4	2	0	6
Both nerve axis and vaginal sheaths	(Seen in two cases at autopsy only)			

TABLE 6

CLASSIFICATION OF METASTASES IN 12 AUTOPSY CASES

	Cases
1. Intracranial	10
a. Brain (pons, cerebrum, cerebellum, meninges, etc.)	10
b. Optic chiasm	3
c. Pituitary gland	2
d. Ventricle	1
2. Extracranial	9
a. Spinal cord	2
b. Viscera:	
(1) Liver	6
(2) Pancreas	2
(3) Spleen	1
(4) Kidney	1
(5) Prostate	1
(6) Lung (Subpleural space)	1
(7) Larger vessels	1
c. Lymph nodes	4
d. Bones	9
3. Both Intracranial and Extracranial	6

Of three fatal cases where the tumor cells were just anterior to the lamina cribrosa, choroidal involvement might explain in two the mode of dissemination, while in one the mother refused enucleation of the second eye in which the nerve and/or choroid might well have been affected.

Mention should be made of the five patients who died but in whom no nerve involvement was apparent. In three, both choroid and sclera were invaded by tumor cells; in one just the choroid; and in another, the vortex veins.

As stated elsewhere in this paper, 20 of the 72 patients are known to have died. In 12* studied at autopsy, metastases were

* An analysis of these 12 cases will be published in another paper.

demonstrated (table 6). Clinical evidence of metastases was seen in six of the eight cases without autopsy.

Case reports

Case 1

Swelling of right preauricular gland, size of golf ball. Presence of tumor cells confirmed by microscopic examination.

Case 2

Patient had symptoms referrable to central nervous system involvement: lethargy, and so forth.

Case 3

X-ray studies revealed changes in left scapula, femur, mandible. Palpable swelling in left scapula.

Case 4

X-ray films showed rarefactions in the right iliac bone and the upper portion of the femur.

Case 5

A huge mass hung from the left orbit down to the shoulder. Face terribly disfigured. Possible intracranial invasion.

Case 6

Large fungating mass from the left orbit. Metastasis was mentioned but not specified.

In two cases, metastasis could have been present, although not evident clinically.

Comment

In this series, as in others reported (Herm and Heath,[12] Griffith and Sorsby,[13] Ingalls[14]), males have been involved more frequently than females both bilaterally and unilaterally. The percentage of bilateral involvement (30 percent) approximates the one-third bilateral involvement estimated by Reese.[10] There were four cases with bilateral involvement in which enucleation could not be done because the patients were in the terminal stage of the disease. If these cases were included in the series, the percentage of bilateral involvement would have been one third.

The average age of onset as previously mentioned was found to be 17.1 months, while the average age at initial treatment was 23.2 months, giving a mean delay in treatment of 6.1 months in this series. With the exception of delay in treatment, these figures are slightly lower than those reported by Falls and Neel[15] (19.9, 25.4, 5.5 months, respectively). This is because symptoms were noted at birth in seven patients.

Unlike those reported by Herm and Heath[12] the survival statistics indicate a sizeable difference between those with bilateral and those with unilateral disease (20 percent). This is explained by the fact that most of the bilateral cases were admitted to Childrens Hospital too late. The fatality in the bilateral cases would have been lower (1) if the delay of treatment had been shortened, or (2) if bilateral enucleation had been done early, or (3) if X-ray treatment had been given early in the remaining eye.

Again, it seems pertinent to emphasize the difficulty in diagnosing a case of retinoblastoma, especially when the media are hazy. Extreme photophobia, conjunctival injection, soft eyeball, unduly large or small eyeballs, absence of calcification, visibility of dentate processes,[10] and eosinophilia—these usually do not favor the diagnosis of retinoblastoma. However, their presence does not necessarily rule out retinoblastoma.

According to Reese,[10] the color of the lesion is an important feature in determining retinoblastoma. Newly formed vessels usually extend over the surface of a pinkish or creamy mass. Moreover, calcium usually can be detected in the lesion by ophthalmoscopy or slitlamp examination with the aid of a Hruby lens (in older children).

Since, in Bedell's[16] words, "Retinoblastoma is an intriguing subject because of the difficulty of early diagnosis (and) the fearful penalty for delay in the treatment . . . ," one should exhaust all the methods and aids in diagnosis before deciding on surgery. I should like, therefore, to present the following steps in a retinoblastoma work-up:

1. As complete a history as possible should be carefully taken, bearing in mind that retinoblastoma is seldom, if ever, an acute process in the beginning. Birth history, family history, and history of the present illness should be included. The signs and symptoms, as tabulated earlier in this paper,

as well as the sequence of their appearance should be recorded and analyzed meticulously. Were there signs of inflammation in or about the eyes before the pupillary reflex was noted, or vice versa?

2. The infant should be examined under ether anesthesia with maximal dilatation of the pupils in both eyes. The examination should include measurement of the corneal diameter, tension-taking, use of a hand slit-lamp, transillumination,* funduscopy, using a giantscope, and Schepen's scope when the vitreous opacities are dense. If there is much corneal bedewing or haziness which cannot be cleared by glycerin, one should even denude the corneal epithelium with a Bard-Parker blade. It should be emphasized that at least two experienced ophthalmologists should examine the child while under anesthesia.

3. X-ray examination for intraorbital calcification and possible changes in the optic foramen should be done routinely. According to Kreibig,[17] no other intraocular tumor shows calcification. However, absence of calcification does not rule out retinoblastoma.

The value of isotope-uptake studies and staining of the aqueous humor according to Papanicolaou's method is questionable. However, in cases in which the aqueous shows clumps of cells (as shown in five cases of this series), staining the anterior chamber fluid may prove fruitful.

In borderline cases, a careful and systematic follow-up and observation should be carried out, during which period more consultations should be held.

Above all, the parents should be dealt with tactfully and kindly. They should be prepared psychologically, and be made to understand that their child is being admitted into a good hospital for further tests and evaluation to help the doctors make a correct diagnosis and arrive at the best method of management. The importance of the time element should be stressed.

After all these steps have been taken and yet retinoblastoma cannot be entirely ruled out, especially if the eye is blind and quite disfigured, enucleation should be done immediately and the eyeball sent to the laboratory for paraffin and celloidin sections. If possible, the patient should be kept in the hospital until the microscopic diagnosis is received, especially regarding evidence of nerve involvement. If this should be present, a team consisting of a neurosurgeon, a pathologist, a radiologist, and the eye surgeon himself, should work in an all-out effort to save the child's life.

The value of early diagnosis cannot be overemphasized because the incidence of nerve, choroidal, and scleral involvement increases in proportion to the delay in initial treatment (enucleation).

Since it is difficult to ascertain clinically which patient has nerve involvement, the surgeon should be sure that at least 10 mm. of the nerve is excised. This can be facilitated by the use of a tonsil snare,[18] or by adequate exposure of the nerve and proper application of the enucleation scissors.

Even cases with signs and symptoms of iritis, like those with muscle imbalance, should be thoroughly studied for possible retinoblastoma.

Finally, what criteria may one use in ascertaining the prognosis of a case? Clinically, the following conditions tend to worsen the prognosis: (1) duration of symptoms for over six months and presence of symptoms at birth: (2) bilaterality of disease; (3) marked corneal enlargement; (4) rapidity of growth of tumor mass; (5) pupils fixed to light, signifying proximity of tumor mass to macular and papillary areas; (6) signs of iritis; (7) any evidence of metastasis; and (8) recurrence of tumor in the orbit after enucleation.

Regarding the histopathologic picture, the following conditions signify gravity of the disease: (1) invasion of the optic nerve behind the lamina cribrosa; (2) presence

* The transilluminator should cast a concentrated beam that can penetrate from behind the eyeball through the sclera, coming out through the dilated pupil, and the examiner's eyes should be dark adapted.

of tumor cells at the very edge of the excised nerve; (3) involvement of the choroid, no matter how slight; (4) presence of tumor cells in the emissary veins in the sclera; (5) presence of retrobulbar or extrabulbar mass; (6) presence of tumor cells on the corneal endothelium; and (7) exophytum type of growth of tumor.

Summary

1. Seventy-two cases of retinoblastoma are reported, 30 percent of which were bilateral.

2. The over-all tumor mortality of the 72 to date is 30 percent, 20 percent of those with unilateral disease and 52 percent of those with bilateral disease.

3. The case fatality is significantly increased by delay of treatment. In other words, the longer the duration of symptoms before initial treatment the higher the mortality rate. Age of onset does not influence case fatality.

4. In bilateral cases, early enucleation of both eyes proved to be the safest procedure. Enucleation of the first eye and early X-ray treatment on the remaining eye was successful in a few cases. When only enucleation of one eye was done in bilateral cases, the mortality was 100 percent. All the four patients having exenteration died, and the only patient with a combined approach suffered the same fate.

5. In unilateral cases, enucleation was the procedure of choice, X-ray therapy being used only when there was evidence of escape of tumor cells into the orbit.

6. Ten cases of misdiagnosis are cited to show how difficult it is to make a correct diagnosis of retinoblastoma.

7. The dimensions of 55 eyeballs harboring retinoblastoma were taken and volumes calculated and the value of 5.8 cc. was found, compared to 6.5 cc. of the normal adult eyeball.

8. Both clinical and microscopic findings carrying a bad prognosis are briefly enumerated.

9. As previously published in the literature,[12] certain data suggest that the longer the tumors exist, the more undifferentiated they become; that is, the fewer rosettes are formed.

635 South Westlake (57).

Acknowledgment

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ACUTE TUBERCULOUS ENDOPHTHALMITIS*

Report of a case

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History

In 1952, H. C., a well-nourished Chinese man, aged 37 years, consulted a physician because he was feeling fatigued and run-down. He also suffered from attacks of asthma. For six months he was treated two times a week with injections of ragweed antigen. Three days after the final injection in the series, his right eye became inflamed and his vision was slightly blurred. Seven days later, on April 21, 1953, he consulted me because of a terrific headache on the right side.

Eye examination

Vision of the right eye was 20/40; left eye, 20/20. The conjunctiva of the right eye was slightly hyperemic and the fundus showed no visible changes. Tension was: R.E., 19 mm. Hg (Schiøtz): L.E., 19 mm. Hg.

Seven days later, vision of the right eye had deteriorated to a blurred 20/200. There was ciliary injection and a beam in the anterior chamber. The vitreous was cloudy and the fundus indistinct.

Three days later vision was reduced to perception of objects and it was impossible to see the fundus.

Treatment

Treatment consisted of atropine, cortigen, streptomycin, and calcium gluconate, but in spite of all treatment the disease progressed.

Course

Three weeks later there was no light perception, tension was hard, and the eye was severely painful. The eye was enucleated on June 15, 1953, two months after onset of blurred vision and pain.

Subsequent history

Four months later, in October, 1953, Mr. H. C., began to feel increasing fatigue. He was irritable and lost weight; in one month he lost 10 to 15 pounds. He began to notice increased pigmentation of the skin; particularly that old scars became darker than the rest of his skin. Three or four times he almost fell asleep while driving his car. Although in the past he had not cared for salt, he began to crave salt and would stop at grocery stores to buy salty foods to alleviate his craving.

In February, 1954, the patient entered Billings Hospital where the diagnosis of Addison's disease was made.

Pathology report on enucleated eye

In the meantime, the enucleated eye was fixed in formalin and processed. Sections showed: The *angles* of the anterior chamber are partially occluded by the iris root.

The *iris* is fibrotic and on its surface is a vascular membrane causing an ectropion. It is firmly attached to the anterior lens capsule by a cyclitic membrane which partially surrounds the lens.

The *ciliary body* is more or less densely infiltrated by inflammatory cells including epithelioid and giant cells. A wide band of granulomatous tissue lines the pars plana.

The *choroid* is infiltrated and tumefied by many confluent tubercles. Some of the tuber-

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cles are necrotic and involve the overlying retina.

The *retina* is edematous and necrotic and is infiltrated with a like cellular picture, especially adjacent to the disc and involving it.

Pathologic diagnosis

The pathologic diagnosis of the eye condition was granulomatous endophthalmitis of unknown etiology.

Course

On May 8, 1954, Mr. H. C. returned to my office to have the vision in his remaining eye checked. During a searching conversation and after several leading questions, the patient recalled that 15 or 20 years earlier, while living in New York, he had had the left kidney removed after an episode of hematuria at the New York Post-Graduate Hospital.

A slide was requested and was found "clearly indicative of tuberculous nephritis." This finding led to the discovery of calcified right peritracheal lymph glands. The tuberculin skin test was positive.

The patient was then treated for active tuberculosis and was given Isoniazid (300 mg. per day), PAS (para-amino-salicylic acid) (10 gm. per day). This therapy was continued until August, 1955. Never at any time has he shown any evidence of pulmonary tuberculosis. The Addison's disease has been well controlled. He is presently taking 37.5 mg. cortisone 2.0 mg. DOCA (desoxycorticosterone acetate), and 2.0 gm. salt per day by mouth.

Review of pathology of eye

Dr. Lorenz E. Zimmerman of the Armed Forces Institute of Pathology volunteered to cut and stain the remaining calottes of the enucleated eye in a search for the etiology of the granulomatous endophthalmitis.

Representative sections were stained with hematoxylin-eosin and for acid-fast organisms. In these slides, Dr. Zimmerman found innumerable typical acid-fast bacilli in the necrotic retina.

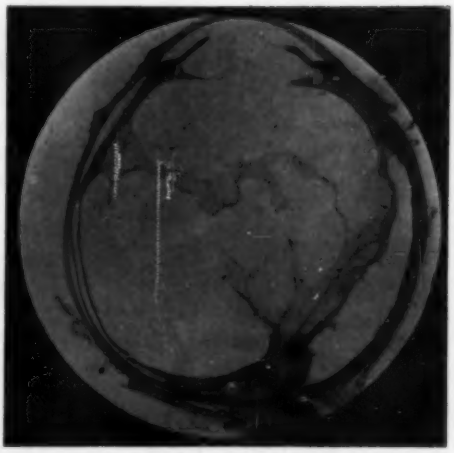

Fig. 1 (Dvorak-Theobald). The whole mount, showing lesions of the choroid breaking through into the overlying retina.

Discussion

Noteworthy in a review of this case is the fact that the patient first sought ophthalmic help three days after the final injection in a six-month course of ragweed desensitization.

It has been pointed out in the literature by a number of authors (for example, Finnoff, Wilmer, Loewenstein, Tobias*) that tubercular lesions may be activated by the injection of tuberculin or such foreign proteins as milk, casein, and so forth.

In the case herein reported, it is possible to trace in retrospect the sequence of events beginning with the desensitization therapy over a protracted period and ending in enucleation of an eye in which tuberculous lesions may have been activated by the foreign protein of the ragweed antigen.

That an activated tuberculosis was not recognized as the etiologic agent at the time of the pathologic diagnosis of granulomatous

* See Duke-Elder, W. S.: Textbook of Ophthalmology. St. Louis, Mosby, 1941, v. 3, p. 2314.

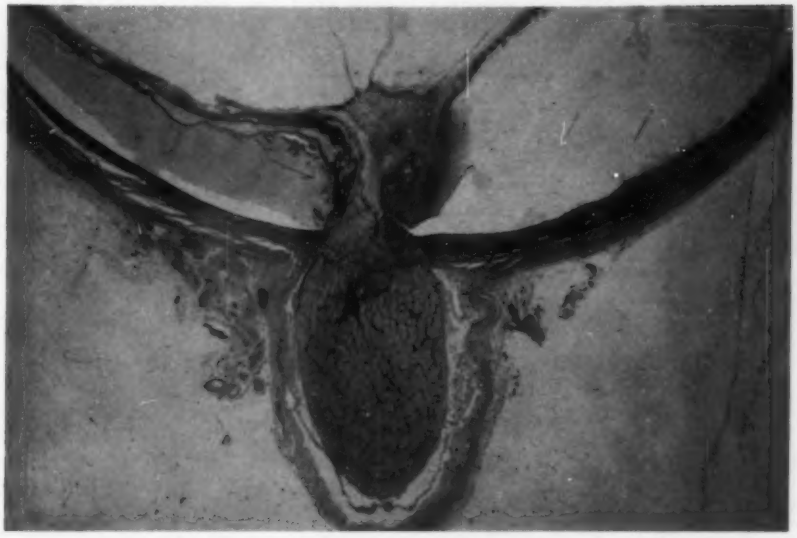

Fig. 2 (Dvorak-Theobald). High-power view of posterior segment, showing infiltration of choroid and lesions of optic nerve.

endophthalmitis was due largely to the fact that tuberculosis was neither suspected nor looked for.

Not until patient probing elicited the history of a nephrectomy for tuberculous nephritis were the eye slides searched for evidence of tuberculosis, the presence of which was verified by Dr. Zimmerman.

As to the classification of the ocular tuberculous lesions, one turns with respect to

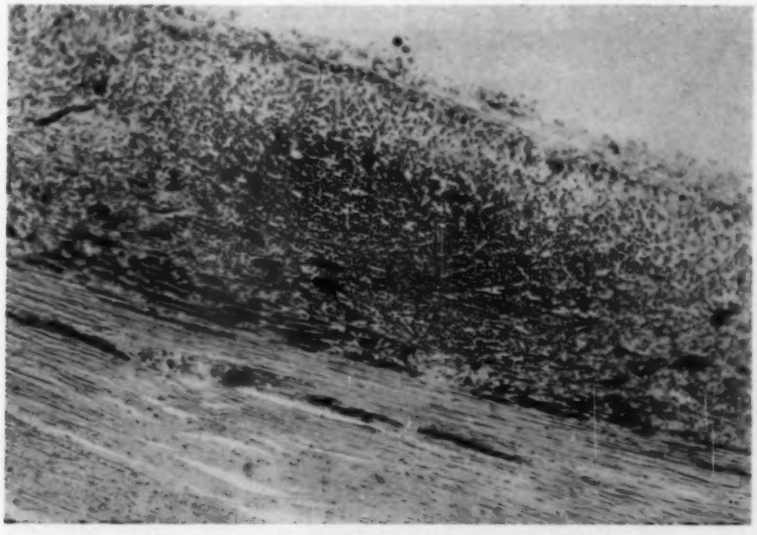

Fig. 3 (Dvorak-Theobald). Tumefaction of the choroid.

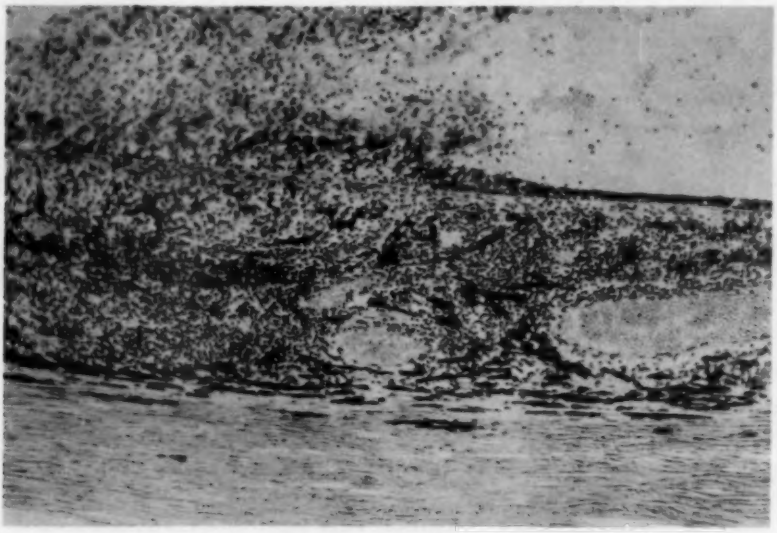

Fig. 4 (Dvorak-Theobald). Granulomatous tissue breaking from the choroid into the overlying necrotic retina.

Alan C. Woods' monumental section on "Ocular tuberculosis" in Chapter 4, "Chronic bacterial infections" in Arnold Sorsby's *Systemic Ophthalmology* (St. Louis, Mosby, 1951, pp. 151-188). On page 165, Dr. Woods says:

> The spreading, devastating form of tuberculous choroiditis . . . is characterized by rapid inflammation and exudations, the process extending from an original small focus which rapidly spreads over the entire fundus and involves the overlying retina.
>
> There is early clouding of the vitreous and destruction of vision. Necrosis and caseation are the rule.

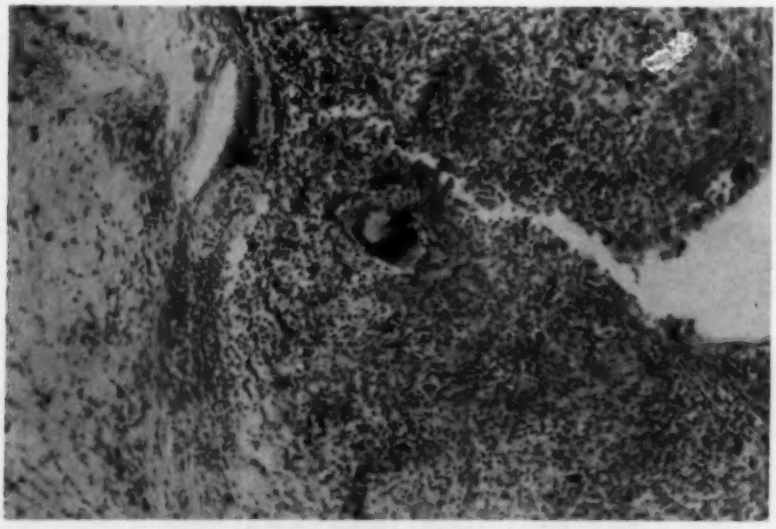

Fig. 5 (Dvorak-Theobald). Granulation tissue in the optic disc, with numerous giant cells.

The illustrations, I believe, can best show that my case fits into Dr. Woods' description of spreading tuberculous choroiditis.

Figure 1, the whole mount, shows choroidal lesions on one side breaking into the overlying retina, the granulomatous infiltration of the optic disc, and inflammatory deposits in the vitreous and lining the retina and ciliary body.

Figure 2 is a high-power view of the posterior segment, showing in more detail the infiltration of the choroid and the granulomatous lesions of the optic disc.

Figure 3 shows tumefaction of the choroid, with granulomatous tissue.

Figure 4 shows granulomatous tissue breaking from the choroid into the overlying necrotic retina.

Figure 5 shows granulation tissue in the optic disc, with numerous giant cells.

Conclusion

Several interesting points are brought out by this case:

1. Probable activation of latent tuberculosis by desensitization therapy, causing a fulminating endophthalmitis.

2. Appearance of tuberculous Addison's disease some months after the eye had been removed.

3. The finding of numerous typical acid-fast bacilli in the necrotic retina cinched the diagnosis of tuberculous endophthalmitis.

715 Lake Street.

ORBITAL BONE INVOLVEMENT

In Besnier-Boeck-Schaumann sarcoid

Nicolas Blatt, M.D., Ursu Alexandru, M.D., Mircea Athanasiu, M.D., I. Muresan, M.D., and V. Popovici, M.D.
Bucharest, Roumania

During the past decade a growing interest has been manifested in the reticulo-endothelial system and particularly in the pathogenesis, morphology, and varying aspects of Besnier-Boeck-Schaumann's sarcoid. Both the symptomatology and histology of this disease have been known for some time but, as knowledge widens, new pathogenetic characteristics are discovered and the generalized nature of the disease is becoming more apparent. At first it seemed to be limited to the skin, then it was learned that the endothelial and ectodermal tissues might also be involved; still later it was learned that it could affect the glands, the ganglions, the respiratory system, the cardiovascular system, and the renal and osseous systems. Indeed, it became known that the principal characteristic of the disease, no matter its location, is that it is a systemic disease of the real reticulo-endothelial system and that it may be present in various organs at the same time.

As time went on more became known about the localization of Besnier-Boeck-Schaumann sarcoid in the eye. Included under Herefordt's disease is the uveitis with many histologic characteristics of this syndrome. There are rare reports of localization of the disease in the lacrimal glands and even more rare reports of its affecting the bony structures of the orbit. Therefore it seemed of interest to report a case in which, although the disease started in the lacrimal gland, it later was localized exclusively in the orbit.

Case report

A school girl, aged 16 years, was examined for the first time on April 11, 1949. There was nothing

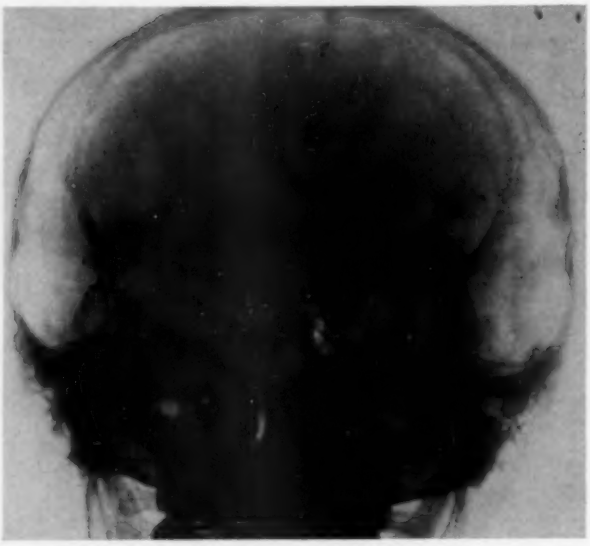

Fig. 1 (Blatt et al.). The radiogram of the skull and orbits. The right orbit, the large wing of the sphenoid, as well as the superior external and external walls of the orbit, are penetrated by a pluricystic tumor, with trabecular zones of osseous formation unevenly distributed.

remarkable in her history. She had had the measles but no other disease that she could remember. She had never suffered from any lung or glandular diseases. Her parents were healthy. No member of her family had ever had tuberculosis. The Bordet-Wassermann reaction of both parents and daughter was negative. The intradermal tuberculin reaction was also negative. X-ray examination revealed no chest or ganglion lesions.

She stated that her present illness had started about a year ago when a small, nonpainful tumor had appeared in the supratemporal region of the orbit. It began to grow, reaching the size of a nut and displacing the globe forward, downward, and inward toward the nose. After examination elsewhere, the condition was diagnosed as sarcoma of the lacrimal gland of the right eye. The gland was removed but the eye continued to be displaced toward the nose. The tumor reappeared but this time on the interior edge of the orbit.

Present examination. When the patient was examined at her first visit (April 11, 1949), the right eye was decidedly exophthalmic. It also showed considerable deviation downward and nasalward. The corneal sensitivity was reduced but the pupillary reflexes were intact.

Fig. 2 (Blatt et al.). Relief radiogram of the right orbit showing an osseous tumor arising from the large wing of the sphenoid.

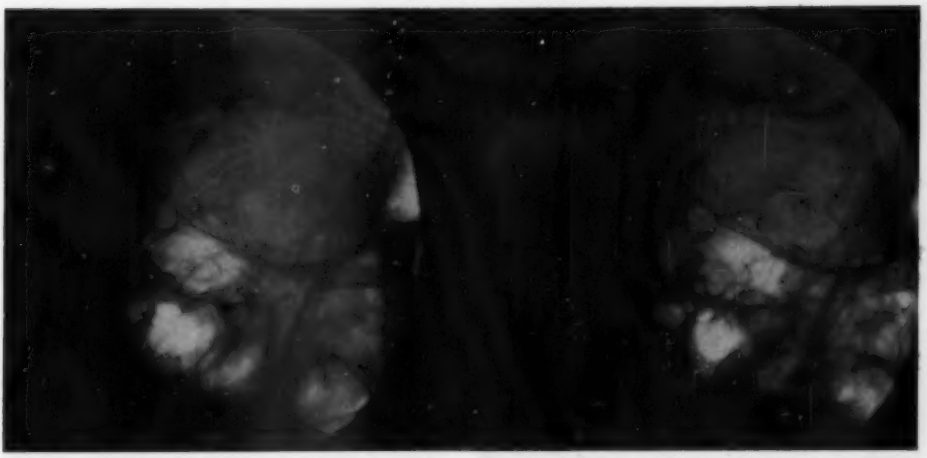

Fig. 3 (Blatt et al.). Relief radiogram of the orbits emphasizing the optic channels. In the right orbit, the anatomic vault of the oval optic channel is intact, has normal dimensions, and an uneroded clear outline.

Fundus examination showed atrophy of the optic nerve, due to compression. Ocular motility was reduced, the globe moving only upward and downward toward the nasal line.

The temporal superior and inferior portions of the orbital arch showed considerable swelling; it had a fusiform aspect. The tegmens seemed almost normal, although they were somewhat inflamed. The appearance of the structures was that of tumefied bone filled with air.

When, several months later, a neuroparalytic keratitis appeared in the amblyopic right eye, with perforation of the globe, the eye had to be enucleated.

Clinically, the diagnosis presented a series of difficulties. The presence of tuberculosis could not be positively eliminated. Energetic antisyphilis treatment, even though tests were negative, did not influence the pathologic process.

Skull radiography and radiography in relief of the orbits, with special attention to the sphenoidal slit and the optic canals, showed:

The large wing of the sphenoid, as well as the superior and exterior walls of the orbit, presented a cystic appearance with unevenly distributed osseous formations in the trabeculae (fig. 1). A lesion which resembled an osseous tumor arose from the large wing of the sphenoid (fig. 2). The optic channels were normal and presented a clear outline, with no erosion (fig. 3).

The left orbit had a normal radiographic aspect (fig. 4).

The radiograms ruled out any tuberculous or syphilitic process. Strict limitation of the neo-

Fig. 4 (Blatt et al.). The left orbit has a normal radiographic aspect.

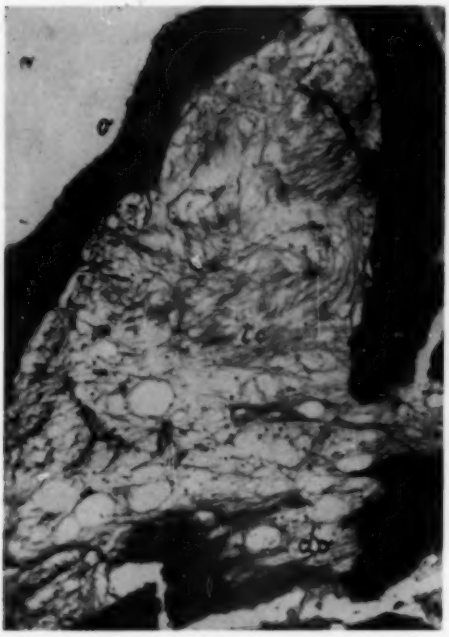

Fig. 5 (Blatt et al.). Osseous rarefaction, with enlarged intertrabecular spaces. (o) Osseous trabeculae. (tc) Conjunctival intratrabecular tissue. There is evidence of bony destruction.

plasm and its localization only in the osseous tissues ruled out malignancy. The cystic formations in the bone and the absence of periosteal lesions seemed to indicate that the disease process was an osseous alteration of the Besnier-Boeck-Schaumann type. Surgery was planned.

Surgery. An incision, the width of a finger and six to seven cm. in length was made parallel to the outer edge of the orbit. It was extended down to the junction of the zygomatic arch with the molar tooth. After the soft parts were sectioned, the outside orbital wall was denuded. The bone seemed clean; its appearance unaltered. In reality, however, it had been reduced to an extremely thin osseous layer which could easily be punctured with a needle. It was as thin as a sheet of parchment.

The bony substance was removed from that portion of the orbital wall which corresponds to the large wing of the sphenoid. No hammer was needed; only a hollow chisel, manipulated with the hand only, and hemostatic forceps. The bony wall of this region, in some places only about one cm. in thickness, was formed of a spongy substance and was dotted with numerous cavities almost equal in size. There were soft formations in these cavities, about the size of a grain of rice, white and necrotic. Some of them were even as large as five to six mm. long and two to three mm. wide. They contained no bony substance, were firmly encapsulated, and did not adhere to the walls of the cavities in which they were found.

There were no openings between the cavities but they were separated by spongy, decalcified layers which were no more than one to three mm. in width. This explains the facility with which the puncturing needle could transverse the bone. Each cavity contained a necrotic, corpusclelike formation.

All these lesions, easily identified by their soft consistency, were removed and a communication was created between the orbital cavity and the temporal zone in such a way that the orbital contents were not disturbed and retained the normal anatomic position.

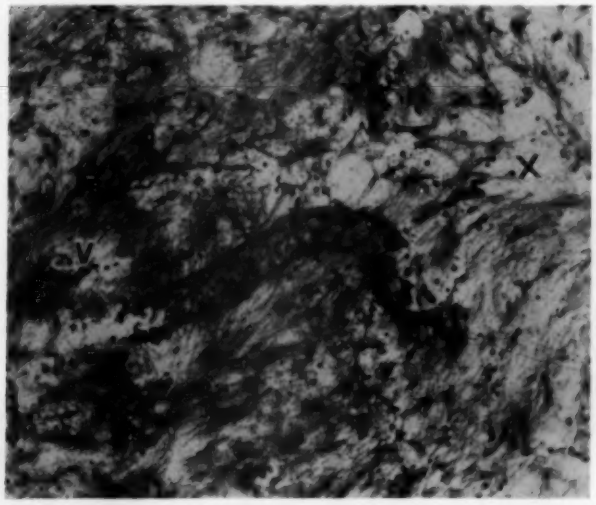

Fig. 6 (Blatt et al.). (X) Conjunctival tissue with (V) newly formed vessels. There is slight, diffuse infiltration with lymphoid elements.

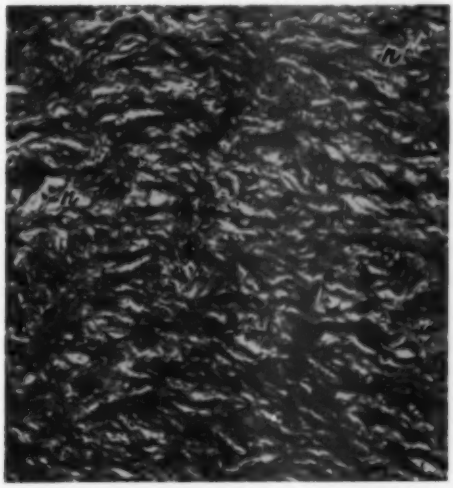

Fig. 7 (Blatt et al.). Sclerosis with hyalinization. (n) Rare nuclei.

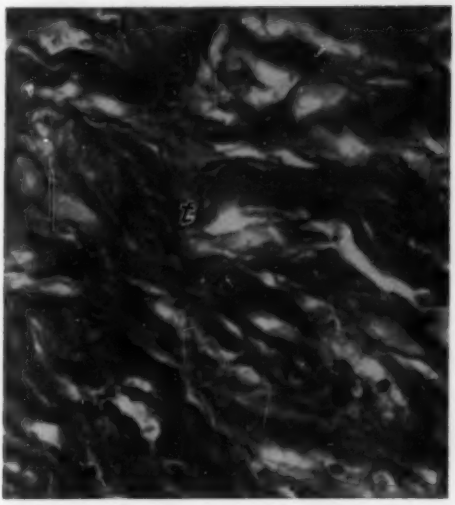

Fig. 9 (Blatt et al.). Intense sclerosis with hyalinization. (t) Anuclear conjunctival tissue.

After suturing, a thin drain was inserted at the lower end of the incision to prevent formation of a hematoma.

Histologic examination

The spongy material and bony formations were sectioned. The bony tissue was rarefied and invaded by small tumors composed of adult vascular conjunctival tissue. It contained bony trabecula with occasional osteoblasts. Its edges were irregular and it contained adult areolar conjunctival tissue with round and oval holes of various dimensions (fig. 5). Small blood vessels appeared here and there (fig. 6). At the periphery of the

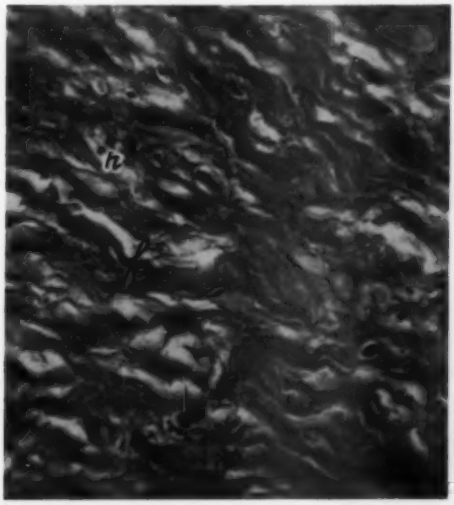

Fig. 8 (Blatt et al.). Internal sclerosis, with hyalinization. (f) Conjunctival fibers. (n) Rare nuclei.

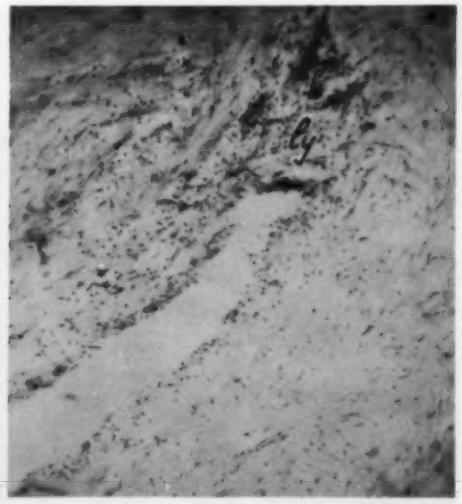

Fig. 10 (Blatt et al.). Conjunctival tissue with numerous waves and blood vessels around (ly) an inflammatory reaction.

Fig. 11 (Blatt et al.). Conjunctival tissue rich in (f) fibrils, with (vs) blood vessels. (ly) Lymphoid perivascular infiltration.

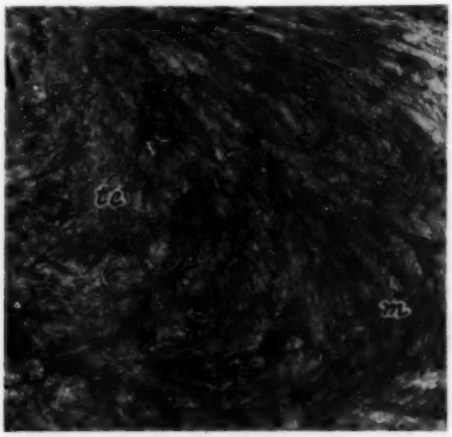

Fig. 12 (Blatt et al.). Conjunctival tissue rich in fibrils and poor in (tc) nuclei. It is arranged in (m) waves.

bony trabecula was a narrow area which showed a slight basophilic reaction. This band, which was contiguous with the intratrabecular conjunctival tissue, was, in places, detached from the substrata. At these points, the bone appeared irregular and pale and harbored destructive lesions (fig. 5).

In other places, the conjunctival tissue was more compact and appeared less mature. It was infiltrated with polyblasts, histocytes, and occasional lymphocytes. It and the bony tissue had no clear-cut demarcation.

The small tumor was composed of numerous collagenous fibers running in different directions. The fibers were extremely hyalinized and contained a few fibroblasts and capillarylike blood vessels of small caliber (figs. 7, 8, and 9). The fibroblasts were more numerous at the periphery than in the center; as were the blood vessels. Present, too, was a discrete perivascular inflammatory infiltrate containing histoid and lymphoid elements (figs. 10 and 11).

Surrounding the tumor was a frame of inflammatory cells, either diffused or in well-

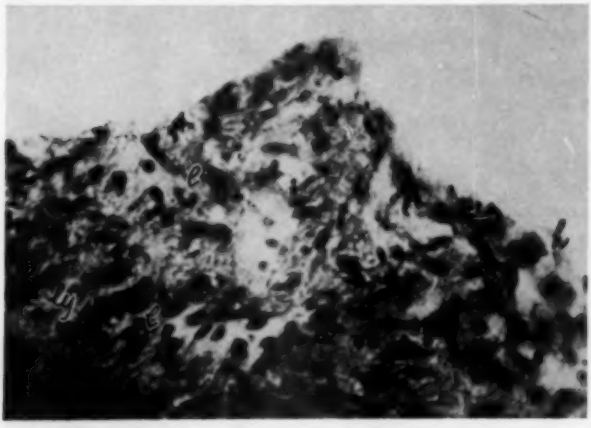

Fig. 13 (Blatt et al.). Productive inflammatory process. (e) Epithelioid type elements. (h) Histiocytes. (ly) Lymphocytes.

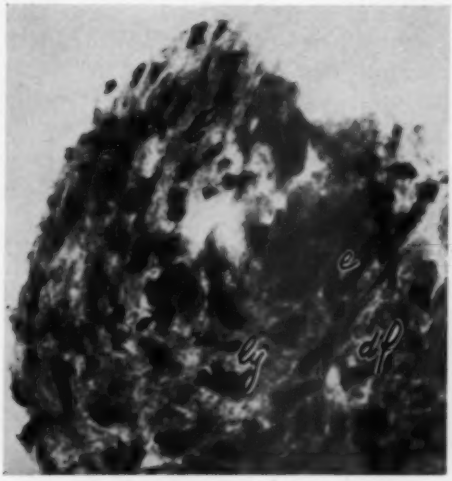

Fig. 14 (Blatt et al.). Proliferative inflammatory process. (e) Epitheliod type elements. (ly) Rare lymphocytes. (df) Fibrinoid degeneration.

Fig. 16 (Blatt et al.). Direct ossification. (o) Osseous tissue. (t) Conjunctival tissue between osseous trabecula. The conjunctival tissue passes directly into the osseous tissue.

limited knots (fig. 12). Under higher magnification, frequent histocytes and polyblasts, with lymphoid elements, could be identified in this zone. In the area of nodular inflammation were groups of epithelioidlike cells, as well as histocytes and occasional polyblasts and lymphocytes (figs. 13 and 14). Dispersed here and there were yellow-brown blood pigments, and fibroid degeneration was present in other areas. The inflammatory nodules were well separated from the conjunctival tissue but there was no surrounding capsule. Figure 15 shows the conjunctival tissue and two calcified nodules surrounded by a slight inflammatory reaction.

Comment

What interpretation should be given to these microscopic findings?

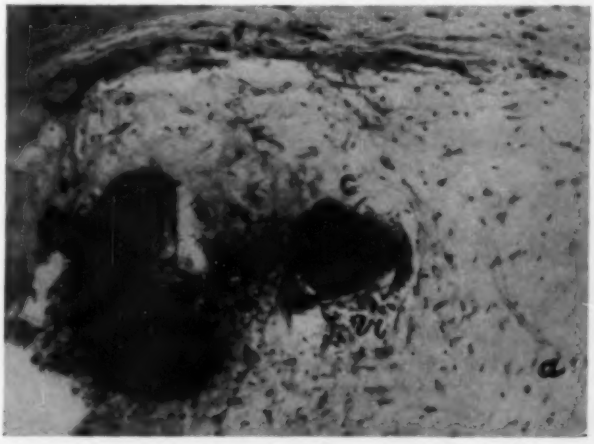

Fig. 15 (Blatt et al.). Conjunctival tissue (a) with calcareous deposits (c). Inflammatory reaction around calcareous deposits (vi).

Considering first the bony formation, one finds definite reabsorption where the bands of conjunctival tissue surround but are not attached to the trabeculae. Here, too, the osseous irregularities penetrate more deeply. In these areas the areolar, intratrabecular adult conjunctival tissue does not present inflammatory infiltration and contains few blood vessels. Elsewhere, however, there is a close connection between the bony formations and the newly formed conjunctival tissue which is more dense, more compact, and seems to have a direct osseous metaphase (fig. 16).

In the area of bony reabsorption, large intratrabecular vascular conjunctival spaces prove the presence of a chronic osteositic process. In other regions, there is osseous destruction.

As for the conjunctival nodule, could it be considered a tumorous fibromatous process?

After considering the peripheral area of greater chronic proliferative inflammation and of the larger number of newly formed vessels, most of which are capillaries, it would appear that this nodule can be nothing but a scar, a sclerotic process, due to a slowly evolving, chronic inflammation.

Microscopic study also confirms that the pathologic process is dominantly a proliferative, inflammatory one. In reality the majority of the peripheral cellular elements may be classed in the reticulo-histocyte system. Lymphoid cells, mobilized or adapted to the inflammatory process, are much rarer. It is confirmed that the histocytes which are grouped in nodules, although their appearance is not too specific, have many of the characteristics of epithelial cells. Moreover, no necrosis is found.

The fibroid degeneration and the deposits of yellow-brown pigment indicate the existence of blood effusion and point to vascular lesions, which also are seen in inflammatory infiltrations, in the walls of some of the small vessels.

Taking into consideration the radiographic aspects, the clinical symptomatology, and the microscopic study of the lesions, one must reach the diagnosis of Besnier-Boeck-Schaumann disease. This, however, is not a typical case with well-encapsulated nodules, formed of epithelioid cells and surrounded with lymphocytes, within an intact abundantly collagenous tissue. Instead, it is an atypical case with rarefying osteosis, old nodules of sclerosis, chronic perivascularization, epithelioid nodules without central necrosis.

Generally the prognosis in this disease is not grave unless, as in the present case, there are secondary alterations, produced by compression or strangulation, which lead to atrophy of the optic nerve or to neuroparalytic keratitis.

Conclusion

In every chronic, slowly progressing inflammation of the ocular and periocular tissues, especially when there are bony alterations, Besnier-Boeck-Schaumann's disease should be considered in the differential diagnosis. Clinical, radiographic, and histologic examinations will permit a precise diagnosis. And it must be emphasized that it is only by co-ordinating these three forms of examination that an exact diagnosis will be made.

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LESIONS OF THE LIDS: A STATISTICAL NOTE*

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Lesions of the lids are an important aspect of the clinical practice of ophthalmology. Many of these lesions are submitted to the laboratory for diagnosis and constitute a large portion of the material studied in the ophthalmic pathology laboratory of the Wilmer Institute. During a study made of the clinical and histopathologic characteristics of such lesions encountered in the laboratory, data accumulated concerning the relative incidences of various lesions, the distribution of these with respect to sex and age, the site of predilection, and the percentages of correct clinical diagnoses. The clinical and pathologic aspects of the lesions can be found in the standard textbooks but the statistical data are infrequently encountered.

The lid lesions submitted during the five-year period between January 1, 1952, and December 31, 1956, were studied. The specimens were contributed by the staffs of the Wilmer Institute and the Baltimore Eye and Ear Hospital, and by a number of outside physicians. All lesions from the lids or from adjacent skin areas were studied. Thus, lesions from the brow and that portion of the nose at the inner canthus were included. Lesions located entirely on the palpebral conjunctiva were excluded. However, this material does not represent a characteristic cross section of diseases of the lids since many lid lesions are not biopsied.

During the five-year period there were 617 such lid lesions. Fifty percent of these were incorrectly diagnosed, illustrating the uncertainty of reliance upon clinical impression alone.

Table 1 illustrates the relative frequency of occurrence of those lesions having an incidence rate of one percent or greater. There were 16 such lesions and 28 other lesions were encountered having an incidence of less than one percent. Among this latter group were sarcoid (0.7 percent), lymphoma (0.3 percent), carcinoma in situ (0.3 percent), amyloid (0.3 percent), mycosis fungoides (0.2 percent), and adenocarcinoma of meibomian gland (0.2 percent).

The papilloma or nevus verucosus was the most frequently encountered lesion, accounting for 20.3 percent of the lesions studied. Clinically it was correctly diagnosed in 70 percent of the cases. Seventy-four percent of the lesions occurred in individuals over 40 years of age. This lesion was equally divided between the sexes and no site of predilection was manifest.

Nevi constituted 14.4 percent of the lesions studied and these were correctly diagnosed clinically in 36 percent of the cases. All decades were represented, though 80 percent of the lesions were in individuals over 30. In 85 of the patients, whose sex was known, the lesion occurred 64 times in the female, suggesting a significantly higher incidence of this lesion in the female. No site of predilection was manifest.

Chalazia, as expected, constituted a large portion of the series, 13 percent. These were correctly diagnosed clinically in 70 percent

TABLE 1

FREQUENCY OF OCCURRENCE

Lesion	Number	Percentage Incidence
Papilloma	125	20.3
Nevus	89	14.4
Chalazion	80	13.0
Basal cell carcinoma	68	11.0
Epidermoid cyst	45	7.3
Dermoid cyst	26	4.2
Epithelial cyst	23	3.7
Xanthelasma	19	3.1
Inflammation	18	2.9
Hemangioma	17	2.8
Basal cell papilloma	16	2.6
Sebaceous cyst	13	2.1
Basosquamous carcinoma	9	1.5
Squamous cell carcinoma	8	1.3
Verruca vulgaris	7	1.1
Hyperkeratosis	7	1.1

* From the Wilmer Ophthalmological Institute of The Johns Hopkins University and Hospital.

TABLE 2

TYPES OF CARCINOMA

Type	Number	Correct Diagnosis (percent)
Basal cell carcinoma	68	56
Basosquamous carcinoma	9	66
Squamous carcinoma	8	50
Carcinoma in situ	2	50
Adenocarcinoma meibomian gland	1	100

of the cases. The lesion occurred with equal frequency in all decades. No sex or site predilection was manifest.

The types of carcinoma encountered along with the percentage incidence of correct clinical diagnosis of each of these are shown in Table 2. The basal cell carcinomas occurred eight times more frequently than either the squamous or basosquamous carcinomas. They were correctly diagnosed clinically in 56 percent of the cases and were most often incorrectly called papillomas, nevi, recurrent chalazia, or cysts.

Grouping all the types of carcinoma together, their age incidence, location, and sex distribution are shown compared with the similar series of Martin in Table 3. In our series the two sexes were equally affected. Only 12.5 percent occurred below the age of 40. The sixth, seventh, and eighth decades had the highest incidence of occurrence (23 percent) which happened to be equal for each of these decades. The lower lid was more commonly involved than either the upper lid or the canthus.

TABLE 3

CARCINOMA OF LIDS

		Martin's Study (147 cases)	Present Study (88 cases)
Sex	Male	57%	48%
	Female	43%	52%
Age	% below age 40 yr.	10%	12.5%
	Most common decade	6th	=6th, 7th, 8th
Location	% Lower lid	54%	57%
	% Upper lid	13%	38%
	% Canthus	33%	5%

TABLE 4

TYPES OF CYSTS

Type	Number	Correct Diagnosis (percent)
Epidermoid	45	4
Dermoid	26	70
Epithelial	23	22
Sebaceous	13	60

The various types of cysts—epidermoid, dermoid, epithelial, and sebaceous—grouped together accounted for 17.3 percent of the lesions. The percentage incidence of correct diagnoses ranged from four percent for the epidermoid cysts to 70 percent for the dermoid cysts (table 4). Aids in the diagnosis of dermoid cysts are factors of age and location. Sixty percent of them occurred in the first decade, and three-fourths of them were either on the brow or upper lid.

The cases of xanthelasma are too few in number, 19, to warrant statistical consideration. However, all of these were correctly diagnosed clinically. Eighty percent of them occurred in individuals over 40 years of age, and the sex distribution, four male, 13 female, two unknown, suggests a higher incidence in the female. Fourteen of the 19 lesions involved the upper lid.

SUMMARY

All the lid lesions, 617, received in the pathology laboratory between January 1, 1952, and December 31, 1956, have been reviewed with respect to incidence of occurrence. In addition, the more frequently encountered lesions—papillomas, nevi, chalazia, cysts, and carcinomas—have been analyzed with respect to site of predilection, and sex and age incidence.

The Johns Hopkins Hospital (5).

REFERENCE

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BILATERAL SIXTH-NERVE PARESIS SIMULATING DIVERGENCE PARALYSIS

AND ITS SURGICAL CORRECTION

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The first case of divergence paralysis was reported by Parinaud[1] in 1883. However, the most complete description of this condition was made by Duane[2] in 1905. There are about 60 recorded cases in the literature, but it is possible that many others are overlooked, misdiagnosed, or pass unrecognized, because little reference to this subject is made in textbooks of ophthalmology or neurology.

The symptoms of divergence paralysis are:

1. Homonymous diplopia, sudden in onset, for distance, beyond 10 to 20 inches.

2. The angle of squint remains the same or decreases slightly on right or left gaze. It increases on downward gaze and decreases on upward gaze, thus the patient tends to depress the chin toward the chest (to minimize the diplopia).

3. Single binocular vision occurs within 10 to 20 inches from the patient (single vision by approximation), and is maintained on right and left gaze.

   a. Single vision maintained when prism base-in of several degrees is placed before the eyes, or

   b. Single vision maintained when the object is slowly carried off again some considerable distance (single vision by recession).

4. Crossed diplopia, due to insufficient convergence, occurs when the image is brought nearer than 10 inches.

5. Normal field of fixation (abduction).

6. Normal accommodation.

7. Normal or diminished amplitude of convergence.

8. Diminished or abolished amplitude of divergence.

9. Constant angle of squint on repeated examination.

10. Base-out prisms for distance give single binocular vision.

The etiology of divergence paralysis may be grouped under the following causes:

1. Inflammatory and toxic diseases of the cerebrum, such as syphilis, tabes, paresis, diphtheria, meningitis, encephalitis, influenza, chorea, poliomyelitis, multiple sclerosis, and lead poisoning.

2. Cerebral hemorrhage.

3. Head trauma.

4. Brain tumor, such as posterior fossa tumors, cerebellar cyst, tumor of vermis, acoustic neuroma, subdural hematoma, tumor of midbrain, hemangioma of the periaquaductal area.

5. Endocrine disorders, such as thyroid disease.

The differential diagnosis of divergence paralysis consists of:

1. BILATERAL SIXTH-NERVE PALSY. Signs of this condition are:

   a. Homonymous diplopia increasing on lateral gaze.

   b. Limitation in field of fixation (abduction) with muscle paretic nystagmus on lateral gaze.

   c. The esotropia may become comitant in a few days and then resemble a divergence paralysis.

   d. An apparent divergence paralysis may later become incomitant and prove to be a sixth-nerve palsy.

2. DIVERGENCE INSUFFICIENCY. Signs of this condition are:

   a. Often no history of sudden development; spontaneous diplopia and other subjective symptoms often absent or little marked.

   b. Angle of squint usually less marked. (0-25 prism diopters).

   c. The amount of diplopia for distance

can be diminished by effort; that is, the patient who at first just sees single with a certain prism is able, by effort, to unite the images with a still weaker prism, base out, or is even able to overcome a prism of one or two diopters base-in.

d. At any given distance the amount of insuperable diplopia is always less than the amount of the screen deviation.

e. The range of single vision on recession of the object is large.

3. CONVERGENCE SPASM. Signs of this are:

a. Abnormal and varying degrees of convergence on repeated examinations.

b. Spastic phenomenon of the near reflex; that is, excessive convergence when fixing at near, intense miosis, functional or spastic myopia.

c. Single binocular vision maintained with base-in prism; that is, once fusion is obtained with base-out prisms, it can be maintained by reducing the base-out prisms even to the point of adding base-in prisms.

d. Neurasthenic or nervous patients with increased irritability combined with abnormal exhaustibility (the patient may have accommodative and convergence insufficiency at reading distance).

4. LATENT ESOTROPIA (ESOPHORIA). The signs of this are:

a. Disrupted fusion by physical or psychic shock.

b. Diminished or absent fusional movements (convergence and vertical vergence as well as divergence).

5. UNCORRECTED ACCOMMODATIVE ESOTROPIA for distance only (according to Urist[17] may simulate divergence paralysis).

COMMENT

The diagnosis of divergence paralysis may be confused with bilateral sixth-nerve paralysis. Theoretically this differentiation should not be difficult. However, when one reviews the reported cases of divergence paralysis, one is impressed with the fact that accurate fields of fixation have been neglected in most of the cases, and many cases of minimal bilateral sixth-nerve palsy are misdiagnosed as divergence paralysis. The examiners merely state that abduction was normal. They base the finding of normal abduction on a gross rotation of the limbus to the lateral canthus, which is not accurate enough to pick up minimal defects in abduction. The normal field of fixation (according to Peter[14] and Duke-Elder[10]) is approximately a 50-degree circle. My experience is that normal abduction is actually about 10 degrees greater than adduction (fig. 1). In any case if abduction is less than adduction when measured on a perimeter, then one must assume the presence of a lateral rectus muscle weakness.

Alger[6] reported nine cases of divergence paralysis and in the three cases (1, 6, and 8) where excursions were measured on the tro-

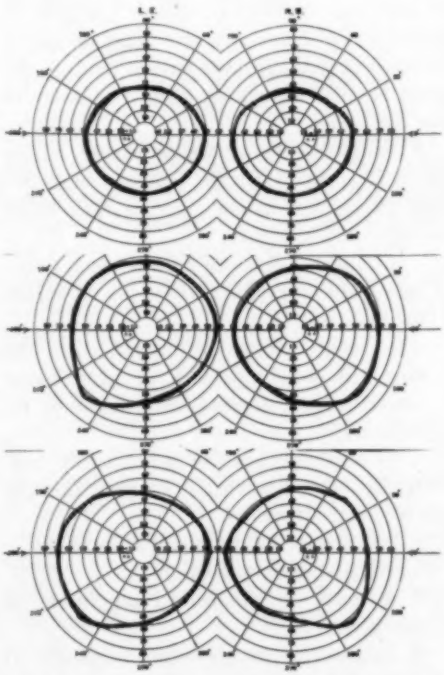

Fig. 1 (Bedrossian). Normal fields of fixation. Top drawing taken from Peter and Duke-Elder. Two lower drawings are from my own experience.

pometer, the abduction measurements were less than the adduction measurements. These findings suggest that the cases mentioned may have been bilateral sixth-nerve paresis rather than true divergence paralysis.

Another finding which is frequently neglected and which is of great diagnostic significance is the presence or absence of horizontal nystagmus on extreme lateral gaze. In true divergence paralysis, nystagmus on lateral gaze should not be present; whereas, in a lateral rectus muscle weakness there would be a muscle paretic nystagmus, present on end-gaze.

A total of 15 cases of divergence paralysis due to increased intracranial pressure,[16] have been reported in the literature. In the four cases reported by Savitsky and Madonick,[3] one case showed a lateral nystagmus and past-pointing. The second case also showed lateral nystagmus when looking to the right and left, and past-pointing of the right upper extremity. Case 3 showed rotary nystagmus on left gaze and past-pointing to the left. Case 4 showed past-pointing to the left and nystagmus in all directions of gaze. All cases were said to have had normal abduction and no weakness of the lateral rectus muscles, and therefore were considered to be divergence paralysis. However, since fixation fields were not done, and since we know that sixth-nerve palsies are common in increased intracranial pressure, there is some question as to whether these cases of so-called divergence paralysis could have been bilateral minimal paresis of the sixth nerves, especially with the presence of nystagmus and past-pointing.

The importance of understanding the syndrome of divergence paralysis is threefold. One must be aware of the possibility of this condition and recognize it as a neurologic entity which may be caused by any of the above-mentioned conditions. Secondly, an attempt should be made to differentiate true divergence paralysis from conditions such as bilateral sixth-nerve palsy, convergence spasm, or a latent esotropia. This is important since the last two mentioned conditions are a functional type of disorder and require conservative therapy, whereas true divergence paralysis and bilateral sixth-nerve palsies are organic in nature, and may therefore require more radical treatment. Finally, once an accurate diagnosis is made more specific treatment can be instituted.

Treatment of this condition is threefold:

1. The underlying cause, if found, must be removed, such as brain tumors or inflammatory and toxic diseases of the cerebrum.

2. Symptomatic relief may be obtained by the patient from base-out prisms to be worn for distance only.

3. Resection of both lateral rectus muscles can be performed if the underlying cause is not found, or if it is a residual and stationary affair from previous inflammatory conditions of the brain.

When one reviews the literature, one finds, surprisingly enough, that very few cases of so-called divergence paralysis have come to ocular muscle surgery. Obviously, those with neurologic disorders should not have ocular surgery until the neurologic condition has become stationary or cured. Many patients are content with symptomatic relief from base-out prism hook-over glasses which are worn for distance only. Therefore, this group either does not consent to muscle surgery or the ophthalmologists do not suggest surgery.

Although some authors suggest resection of both lateral rectus muscles to correct this condition, I was able to find only one report (Urist[17]) in the literature of such surgery being performed for this type of case. Theobald,[4] in 1886, operated on a patient with homonymous diplopia by performing bilateral tenotomy of each medial rectus muscle. He apparently obtained correction of the diplopia for distance, although there was some question as to the original diagnosis.

Uthoff,[5] in 1893, also performed a tonotomy of one internal rectus muscle with apparently good results. Sachs,[6] in 1898, re-

corded two patients on whom operations were performed. In one case he did an advancement of the external rectus muscle and claimed postoperative single binocular vision. In the second patient the internal rectus muscle was tonotomized and the patient had single vision postoperatively. However, one week after surgery it was necessary to use a 10-diopter prism base-out, to relieve the diplopia for distance, and a four-diopter prism base-out to relieve the diplopia for near.

Von Hippel[7] also operated on a case in 1902 in which he did a tonotomy of the internal rectus muscle for 20 degrees of esotropia. However, postoperatively, although there was single binocular vision in eyes front, there was a crossed diplopia on lateral gaze which suggests a postoperative paralytic divergent squint on lateral gaze.

If operative procedures are to be instituted, it is difficult to understand why weakening of either medial rectus muscle should receive any consideration for a condition such as divergence paralysis or minimal bilateral sixth-nerve paresis. If accurate measurements are made and a definite diagnosis is established, it would seem more rational to perform a strengthening operation on both external rectus muscles in this type of case.

Case reports

Case 1

Mrs. A. M., aged 49 years, was first seen on May 26, 1954, at which time she complainted of horizontal diplopia for distance only, for the past three years. Her vision was correctible to 6/6 in each eye, and she was found to be wearing 8.5 diopter base-out prisms incorporated in her glasses. Her muscle examination showed 15 diopters of esotropia at distance which was the same on right and left gaze, and which became less in amount by approximation to 40 cm., at which point she had single binocular vision. As the object was brought nearer to the nose, the cover test showed an exo movement. Fusion studies on the synoptophore showed 35 diopters of convergence and 15 diopters of divergence ability.

Fundus examination and visual field studies were normal. The patient showed a definite pathologic horizontal nystagmus on right and left lateral gaze, and also a vertical nystagmus on upward gaze.

The patient was known to have hypothyroidism and was on thyroid medication. When she did not take her medication faithfully her eyes seemed to feel worse.

Grossly, the patient did not appear to have any weakness of abduction, but when her fields of fixation were carefully plotted she was shown to have an impairment in abduction of both lateral rectus muscles. She also was aware of dropping her chin in order to see more comfortably. She was given 12-diopter base-out prism hook-overs to be worn just for distance, and not for near, since this was the minimal amount of prism which relieved her diplopia for distance. The patient wore this correction comfortably for one year (until May 27, 1955), at which time she consented to have muscle surgery done, since she felt that the hook-over prisms were too much of a nuisance and inconvenience.

The patient was admitted to the Graduate Hospital, Philadelphia, for a complete neurologic and neuro-otologic study. Neurologic examination was completely negative except for the eye findings. X-rays of the skull, sinuses, teeth, and chest were negative. An electroencephalogram showed a few minimal slow waves but the consultant felt that this was normal. Calorie stimulation tests showed no pathologic alteration in the median longitudinal bundle, although she did show a lack of sensitivity on both sides, which, however, was of no localizing value.

Since these studies were all negative, it was decided to proceed with the muscle surgery, and on June 16, 1955, an eight-mm. resection of both lateral rectus muscles was performed. Immediately following surgery she had a large exo at distance and crossed diplopia, which disappeared two days later.

Fixation fields repeated seven weeks after surgery and again two years after surgery showed an increase of 10 to 15 degrees of abduction of either eye (fig. 2). However, the nystagmus was still present as before. Three months following surgery and two years later, the patient was orthophoric at distance, and showed a slight exo of four diopters at near. Her near-point of convergence was six cm. The patient showed no diplopia on right or left gaze at either distance or near, and it should be pointed out that the postoperative measurements were concomitant for distance and near, and that the near-point of convergence was not impaired by surgery.

Case 2

Mr. P. K., aged 19 years, was first seen in consultation on June 15, 1955. He complained of double vision at distance only, for a duration of one year. His double vision seemed to be slightly more apparent on left gaze and was more troublesome in the past six months. His vision was correctible to 6/6 in each eye. Muscle examination showed 16 diopters of esotropia and homonymous diplopia at distance, which was slightly worse on

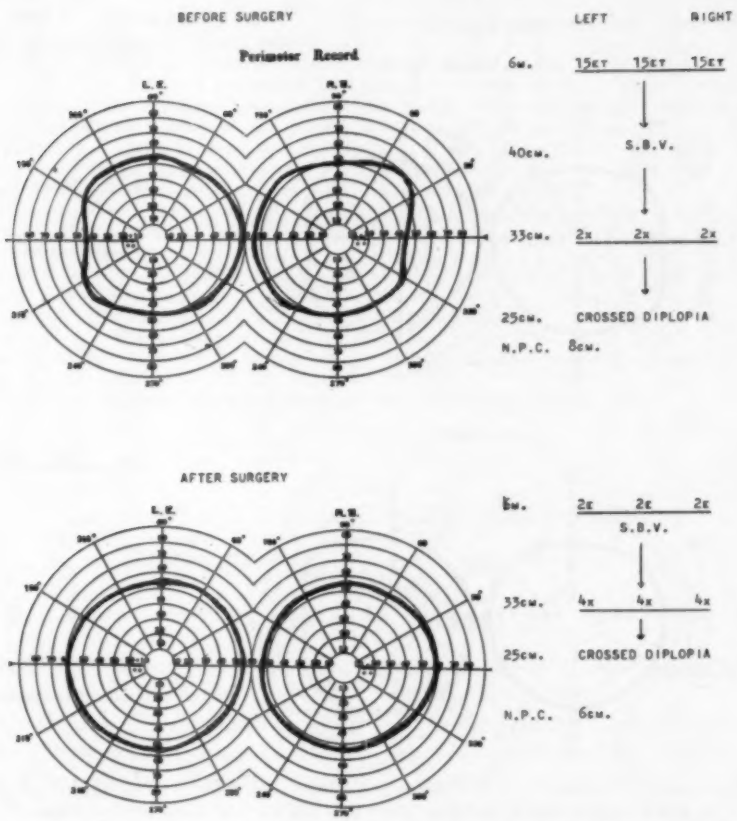

Fig. 2 (Bedrossian). Fixation fields and corresponding red-glass diplopia fields before surgery and two years after bilateral resection (eight mm.) of the lateral rectus muscles.

left lateral gaze. The diplopia decreased to single vision by approximation at 48 cm. from the nose and was maintained to seven cm. from the nose. Within seven cm. he showed a trace of exo with crossed diplopia. His absolute near-point of convergence was four cm. Fusion studies on the synoptophore showed 40 diopters of convergence and 10 diopters of divergence ability. The patient had horizontal nystagmus on right and left gaze, slightly more marked on left gaze. Fixation fields showed bilateral limitation of abduction, slightly more marked on the left (fig. 3).

Since complete neurologic evaluation was negative except for the eye findings, it was advised that he have a bilateral resection of both lateral rectus muscles. However, only a resection of the left lateral rectus muscle (eight mm.) was performed on June 21, 1955. The preoperative and postoperative findings are summarized in Figure 3. It can be seen that a unilateral resection of the left lateral rectus muscle improved the abduction, and reduced the esotropia at distance primarily on left gaze, but hardly altered the measurements at distance on right gaze. The near measurements were not affected, as one would desire, since these were normal before surgery. It can be seen that more adequate correction would have been obtained if the right lateral rectus muscle was also resected. This, however, can still be done as a second procedure.

Summary

The cases presented show how a minimal bilateral sixth-nerve weakness may simulate a divergence paralysis except for the presence of nystagmus and limitation of abduction only brought out by plotting fixation fields. These cases had muscle surgery performed according to sound operative reason-

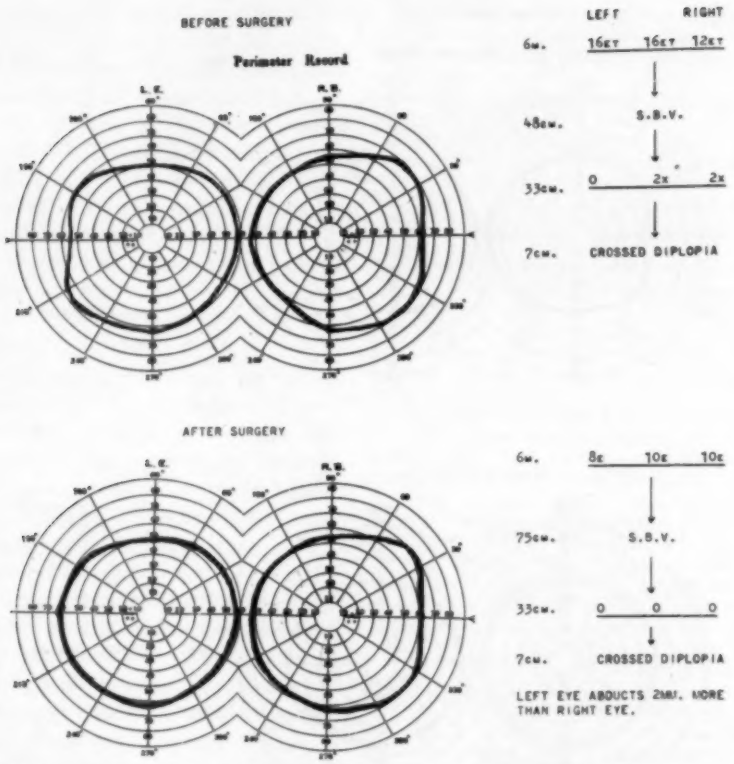

Fig. 3 (Bedrossian). Fixation fields and corresponding red-glass diplopia fields before surgery and two years after unilateral resection (eight mm.) of the left lateral rectus muscle.

ing. The first case had adequate bilateral surgery, whereas the second case had insufficient unilateral surgery.

The excellent result of the surgery performed bears out the important surgical principles involved by operating on the muscles of divergence. The limited abduction has been improved and the deviation has been kept a comitant one as it was to begin with in the first case. Also the muscles of convergence have not been tampered with in any way, and the position of the patients' eyes in the near position were not altered whatsoever. This is an extremely important point, especially in persons of presbyopic age where the exophoria of presbyopia could be made much worse if the medial rectus muscles were weakened by an operation.

It is hoped that in the future, cases of this type will be reported with more accurate diagnostic studies, since one should expect a better surgical result in cases of minimal bilateral sixth-nerve palsy by improving defective abduction. On the other hand, one would not expect as good a surgical result in true divergence paralysis, since this condition is a supranuclear defect with normal abduction to begin with.

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MORPHOLOGY OF INCLUSION BODIES*

In trachoma and inclusion conjunctivitis

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Prowazek-Halberstaedter inclusion bodies have a diagnostic value in cases of acute trachoma and inclusion conjunctivitis. The diagnosis of these two diseases is confirmed by the presence of the Prowazek-Halberstaedter bodies in the epithelial scrapings. However, in cases with Prowazek-Halberstaedter bodies in the scrapings, the trachoma is not necessarily acute but often chronic, with superimposed bacterial infection. Accordingly in the diagnosis of acute conjunctivitis the examination of the epithelial scrapings is indispensable to the clinical picture and bacteriologic examination of the smears.

I. Preparation of epithelial scrapings

1. Taking the scrapings

The scrapings for demonstrating Prowazek-Halberstaedter bodies should be taken from the area of the conjunctiva showing the most marked lesions, especially from the surface of the follicles.

The conjunctiva is anesthetized, the eyelids are everted, and the surface discharge is removed. The conjunctiva is scraped with the edge of a cover-glass, which is thin and about 18-mm. square. In the acute stage of trachoma, pressure should be deep enough to cause slight bleeding; while in the chronic stage it should be light and not deep enough to cause bleeding. The material should be spread on a clean glass slide as thinly as possible and should not be pressed against the slide or nuclear extrusions may result. From each case four slides should be prepared from the lower and upper conjunctivas of both eyes.

The scrapings are dried in air and fixed in absolute methyl alcohol for two minutes.

2. Staining

Giemsa stain is the most satisfactory method for detecting Prowazek-Halberstaedter bodies.

The slides are flooded with diluted Giemsa

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solution, in the proportion of one drop of the Giemsa solution to two ml. of distilled water, and are covered with a dish and stained for 30 minutes. After being washed thoroughly with tap water, they should be dried as quickly as possible by placing a piece of filter paper at one end and blowing hard.

A freshly prepared mixture of Giemsa stain of good quality should be employed. Mixtures containing coarse particles of the stain are inferior. Thick films cannot be stained in fine detail. Films should be fixed and stained as soon as possible after taking the scrapings.

3. Examination

The examination of the scrapings is begun under low power (×10) with a ×10 eyepiece. If any cells show changes in the cytoplasm, the cells in question are observed under an oil immersion lens. The entire slide should be examined and every suspicious cell should be examined under an oil immersion lens.

When Prowazek-Halberstaedter bodies are examined, the following considerations must be kept in mind: the principal object in view is the elementary bodies. The initial bodies are occasionally difficult to differentiate from other nonspecific granules and bacteria. When the initial bodies are found, Prowazek-Halberstaedter bodies composed of elementary bodies are also always present. Accordingly the decision that Prowazek-Halberstaedter bodies are present should be based on the finding of typical Prowazek-Halberstaedter bodies composed of elementary bodies. The secret of success in detecting Prowazek-Halberstaedter bodies in the conjunctival scrapings lies (1) in the preparation of good films, (2) in perseverance in examining the films, and, (3) in experienced observation.

II. Morphology of Prowazek-Halberstaedter bodies

Prowazek-Halberstaedter bodies consist of small particles and a matrix. The small particles are elementary bodies, initial bodies, free initial bodies, free elementary bodies, and residual bodies. The matrix is a plastin-like substance and carbohydrate.

The morphology of Prowazek-Halberstaedter bodies in the epithelial scrapings stained by Giemsa's method is:

1. Elementary body

Elementary bodies are the elementary component of Prowazek-Halberstaedter bodies and represent the morphologic unit of the trachoma virus and are considered as the infective unit of the virus. They are sharply defined, round, reddish-blue granules having a diameter of approximately 0.25 μ. They are uniform in size and form. However, the staining reaction may vary from red to purplish blue according to the stage of the development. The elementary bodies observed in Prowazek-Halberstaedter bodies in an early stage are purplish blue, while those in a regressive stage are red.

2. Initial body

Initial bodies appear in large numbers in the early stage of Prowazek-Halberstaedter body formation. Accordingly, they are abundant during the early stage of acute trachoma and inclusion conjunctivitis. They are round or oval. They stain dark purplish-blue and are uniform in their staining reaction. However, they vary greatly in size, having a diameter of 0.4 to 1.2 μ, occasionally 1.5 μ in the longest diameter. They are usually arranged in pairs and frequently in a "morula" pattern.

All the stages of transition between elementary and initial bodies are clearly observable.

3. Free initial body

Free initial bodies are initial bodies arranged in pairs and scattered in the secretions, in a free state, outside conjunctival epithelial cells.

4. Free elementary body

Free elementary bodies are in a free state and are scattered in the secretion because of

rupture of the cell membrane. They enter epithelial cells and multiply to form Prowazek-Halberstaedter bodies. Rupture of the cell membrane, with consequent liberating of elementary bodies into the secretion, is often observed. The free elementary bodies, immediately after liberation, are usually surrounded by a light-blue stained, amorphous matrix.

5. Residual body (Restkoerper)

Residual bodies appear in Prowazek-Halberstaedter bodies in a regressive stage. They stain red and are round, larger granules, being approximately the size of the initial bodies.

6. Matrix

a. *The plastinlike substance* stains blue and is amorphous. The elementary and initial bodies lie embedded in it. It appears most abundantly in the early stage of Prowazek-Halberstaedter body formation. As the bodies grow larger, the plastinlike substance fades and becomes clear and unstained. However, it is occasionally demonstrated abundantly in mature large Prowazek-Halberstaedter bodies, and stains light red in the regressive stage associated with residual bodies.

b. *The polysaccharide matrix.* In 1936, Rice[1] reported that Prowazek-Halberstaedter bodies have a carbohydrate matrix which gives a glycogen staining reaction with a compound solution of iodine. I employed the PAS (periodic acid-Schiff) reaction as a method for histochemical demonstration of polysaccharide. From the results obtained the term "polysaccharide matrix" is offered. Various modifications of the PAS reaction have been used.[2, 3, 4]

The Lillie method is the best for demonstrating polysaccharides:

1. Scrapings are fixed in methyl alcohol for two minutes.
2. Immerse in Lillie's oxidizing agent for 10 minutes. Composition of the mixture: potassium or sodium periodate, 0.8 gm.; 70-percent nitric acid, 0.3 ml.; distilled water, 100 ml.
3. Wash for five minutes.
4. Place in Schiff's reagent for five minutes.
5. Rinse the reagent off in a M/20 solution of sodium metabisulfite three times for five minutes in all.
6. Wash for 10 minutes.
7. Counterstain with iron hematoxylin and picric acid for two to three minutes.
8. Wash and dry.

Lillie's oxidizing agent and Schiff's reagent should be prepared immediately before use.

The results show that Prowazek-Halberstaedter bodies generally give a positive PAS reaction, demonstrating that they contain polysaccharide in the matrix. In general, the mature and developing forms give a highly positive PAS reaction and contain a large quantity of polysaccharide, while the immature forms give a slightly positive or a negative PAS reaction and contain a small amount of polysaccharide (figs. 1 and 2).

Mature Prowazek-Halberstaedter bodies of the elementary body type give an intensely positive PAS reaction. Their matrix is stained red all over, and more deeply stained corpuscles are observed. Occasionally there are unstained round cavities, having the appearance of a honeycomb, between these corpuscles. These corpuscles and cavities do not correspond with the elementary bodies demonstrated by Giemsa stain.

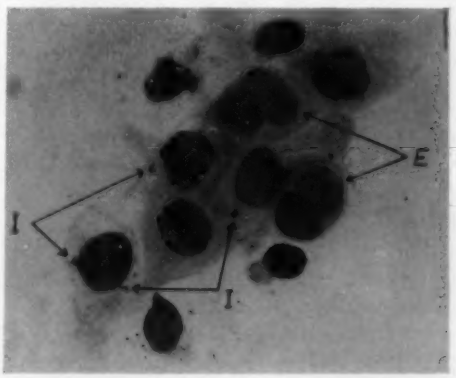

Fig. 1 (Mori). Large mature Prowazek-Halberstaedter bodies of the elementary body type (E). Small immature Prowazek-Halberstaedter bodies of the initial body type (I). (Giemsa stain, ×1,000.)

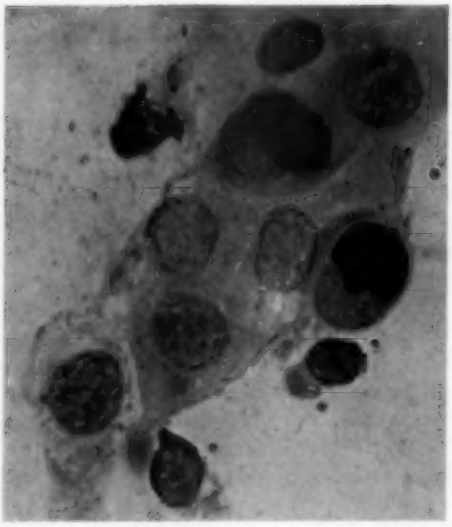

Fig. 2 (Mori). The slide of Figure 1 was decolorized and then restained by the Lillie method. Prowazek-Halberstaedter bodies of the elementary body type (E) give an intensely positive PAS reaction, while those of the initial body type (I) give a negative PAS reaction.

The matrix of small Prowazek-Halberstaedter bodies, consisting of a small number of elementary bodies, has small red corpuscles, not staining all over, which are glycogen granules.

The free elementary bodies scattered outside conjunctival cells are PAS negative, but those surrounded with amorphous ground substance, which have just been liberated from the host cell, are slightly PAS positive.

Prowazek-Halberstaedter bodies of the initial body type give a slightly positive or a negative PAS reaction. They contain a smaller amount of polysaccharide than the inclusions of the elementary body type.

The free initial bodies are PAS negative, and Prowazek-Halberstaedter bodies of the initial body type in the "morula" stage are usually negative and occasionally slightly positive. Even intermediate and large inclusions of the initial body type are negative under certain circumstances, but on occasion partially positive.

The polysaccharides of Prowazek-Halberstaedter bodies differ from the plastinlike substance. Prowazek-Halberstaedter bodies which do not show plastinlike substance with Giemsa stain give a positive PAS reaction, and the quantity of plastinlike substance does not correspond to the degree of positivity of the PAS reaction; however, Prowazek-Halberstaedter bodies which have a large amount of plastinlike substance are inclined to have a large quantity of polysaccharide.

The saliva test for glycogen was performed. Glycogen is digested by saliva so there is a negative PAS reaction. If the matrix contains polysaccharides other than glycogen, the reaction remains positive after the saliva test.

The slide is placed in saliva (filtered and diluted 4:1 with phosphate buffer at pH 7.0) for one hour in an incubator at 37°C. After washing, it is stained by the Lillie method.

The polysaccharide matrix mostly disappears but a partial positive reaction remains and, occasionally, it remains unchanged. This remaining polysaccharide matrix also stains, showing granules.

These results show that the matrix of Prowazek-Halberstaedter bodies contains glycogen and another polysaccharide in addition to glycogen.

III. Azurophilic reticular inclusion bodies

Azurophilic reticular inclusion bodies are demonstrated in the cytoplasm of the conjunctival epithelial cells and are stained light red with the Giemsa stain. They consist of a filamentous or reticular structure. The filament is very thin and is dotted with knots, which are almost equal in size to the elementary bodies. On rare occasions relatively thick filaments are observed, which are stained purplish red and are approximately 0.2 mμ in width; they are almost equal in diameter to the elementary bodies (figs. 3 and 4).

The azurophilic reticular inclusions appear near the nucleus and in the central part of

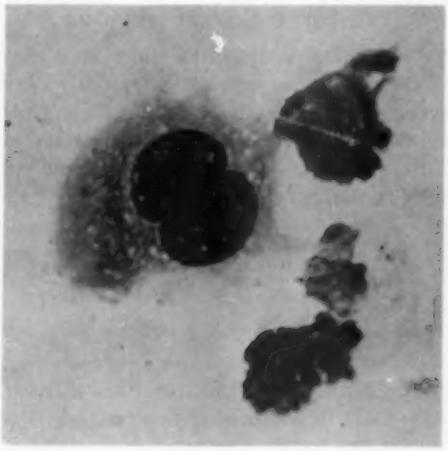

Fig. 3 (Mori). The azurophilic reticular inclusion bodies. (Giemsa stain, ×1,500.)

the cytoplasm. They are demonstrated in the early stage of acute trachoma; they are found during the first week and most abundantly on the third, fourth, and fifth days after the onset.

In the beginning of the disease the conjunctival epithelial cells containing azurophilic inclusions are more abundant than the cells with Prowazek-Halberstaedter bodies which are not found in cells containing azurophilic inclusions. Thereafter, however, Prowazek-Halberstaedter bodies in an early stage of development appear from the azurophilic inclusions and both inclusions are found in the same cell. In these cases the Prowazek-Halberstaedter bodies are small and in an early stage of inclusion formation; several elementary bodies appear from the filament of the azurophilic inclusions, which fade and disappear, losing their azurophilic staining reaction. Elementary bodies appear in the area where the filament has disappeared (figs. 5 and 6).

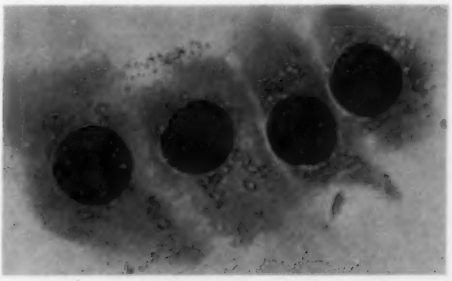

Fig. 4 (Mori). The azurophilic reticular inclusion bodies are seen in each cell. (Giemsa stain, ×1,500.)

As the Prowazek-Halberstaedter bodies grow larger, the azurophilic inclusions fade and disappear completely. On the seventh and eighth days after onset, many large mature Prowazek-Halberstaedter bodies are demonstrated and the azurophilic inclusions disappear and are never seen again.

Thus, it would seem that azurophilic re-

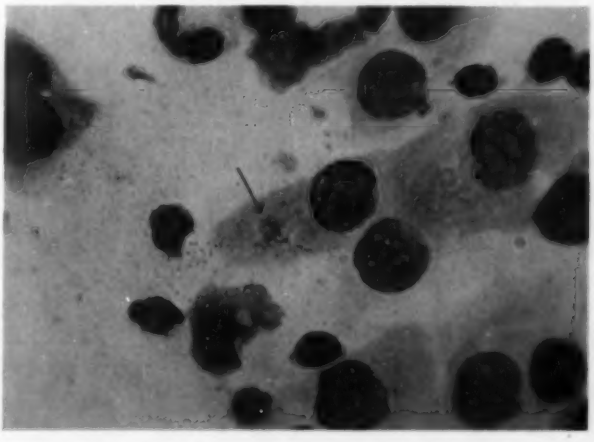

Fig. 5 (Mori). The azurophilic reticular inclusion bodies give rise to Prowazek-Halberstaedter bodies consisting of several elementary bodies (arrow). (Giemsa stain, ×1,500.)

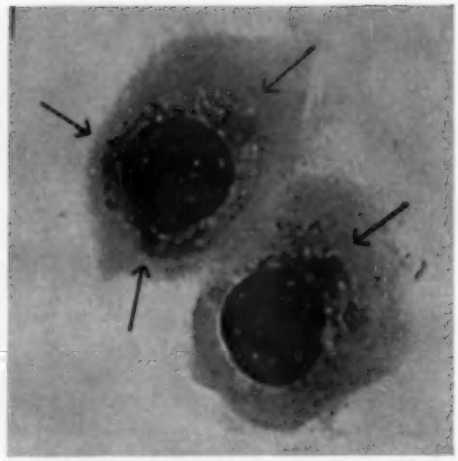

Fig. 6 (Mori). Prowazek-Halberstaedter bodies grow larger (arrows), and the azurophilic reticular inclusion bodies fade and become smaller. (Giemsa stain, ×1,500.)

ticular inclusions are closely related to Prowazek-Halberstaedter bodies. They may represent the stage of the immature virus, which is formed before the stage of the appearance of the visible elementary or initial body particle in the sequence of development from the free elementary body to Prowazek-Halberstaedter body formation. The immature virus or provirus is an invisible vegetative virus and ripens to become an infective, complete, mature virus.

The azurophilic inclusions are also demonstrated at the beginning of inclusion conjunctivitis. They are found during the first three days after the onset of the disease in newborns. They are morphologically identical with those of trachoma. These azurophilic inclusions show negative Feulgen and PAS reactions and no metachromasia with toluidine-blue staining. Moreover, azurophilic inclusions are occasionally found in small numbers at the beginning of epidemic keratoconjunctivitis. They are very few but appear morphologically identical with those of trachoma and inclusion conjunctivitis. This seems to indicate that epidemic keratoconjunctivitis is caused by a virus.

IV. Toluidine-blue staining

The normal conjunctival epithelium contains varying numbers of goblet cells. They occur most frequently in the fornices. They usually have homogeneous blue masses in their cytoplasm with the Giemsa stain, but their appearance varies according to the state of mucin formation; they appear occasionally as a granular mass. The granules are stained reddish purple and vary in size and form.

As goblet cells show a somewhat similar appearance to Prowazek-Halberstaedter bodies[5-7] and give a positive PAS reaction, they could be confused with Prowazek-Halberstaedter bodies. They can be clearly identified by toluidine-blue staining.

Goblet cells contain mucopolysaccharides. Mucopolysaccharides show metachromasia when stained with a buffered solution of toluidine blue. Metachromasia is characteristic of the histochemical demonstration for mucopolysaccharide.[8,9] The method is:

1. Scrapings are fixed in methyl alcohol.
2. Immerse in one-percent solution of toluidine blue in a buffer of pH 3.2 (15 parts M/10 citric acid to five parts M/5 disodium hydrogenphosphate) for one hour.
3. Differentiate in 70-percent alcohol.
4. Wash.

Goblet cells in the conjunctiva have metachromasia at pH 3.2; the nucleus is blue and mucopolysaccharide is purple. At pH 2.5 goblet cells show no metachromasia and at pH 4.1 the nucleus stains purple. Therefore, staining at pH 3.2 is the most satisfactory. Prowazek-Halberstaedter bodies present no metachromasia at pH 3.2. Azurophilic inclusions also have no metachromasia.

V. Feulgen reaction

The procedure of the Feulgen reaction is so complicated and delicate that the results obtained often vary with different workers.[10-13] I have devised a procedure which gives a satisfactory result with the Feulgen reaction in the scrapings. It is as follows:

1. Immerse in cold 1 N hydrochloric acid for one minute.

2. Hydrolyse with 1 N hydrochloric acid at 50°C for 15 minutes.
3. Wash in cold 1 N hydrochloric acid for one minute.
4. Immerse in Schiff's reagent for two hours.
5. Rinse in a bleaching solution (1 N hydrochloric acid, five ml.; 10 percent kalium metabisulfite, five ml.; distilled water, 100 ml.) three times for 10 minutes each.
6. Wash under the tap for five minutes.

Prowazek-Halberstaedter bodies show a slightly positive Feulgen reaction. It is more difficult to produce the reaction in scrapings than in sections. Accordingly great caution is required in developing the reaction and in the evaluation of the results.

VI. Discussion

It is very important that the azurophilic reticular inclusions are demonstrated in the early stage of acute trachoma and inclusion conjunctivitis. Azurophilic inclusions are closely related to Prowazek-Halberstaedter bodies and represent a stage in the development of the virus.

Since Dohi[16] demonstrated DNA in the azurophilic inclusions of ectromelia virus, the azurophilic reticular inclusions are considered to be composed of DNA, which seems to be produced during the metabolic process of the host cells and to be used as material for virus nucleic acid before the stage of the completion of the elementary bodies. Microscopically, the azurophilic reticular inclusions show a negative Feulgen reaction, in spite of containing DNA as their principal constituent. It may be difficult to demonstrate a positive Feulgen reaction because of the small amount of DNA, since azurophilic reticular inclusions are very minute structures.

Azurophilic reticular inclusions are considered to represent a stage of the immature virus or provirus. The immature virus is an invisible vegetative virus and ripens to become the infective complete mature virus—the elementary body. The immature virus of bacterial viruses, especially T_2 phage, has been studied systematically by means of the electron microscope,[17] and immature animal viruses have also been demonstrated by the electron microscope.[18]

The elementary body disappears after penetrating the cell membrane. This stage is called a dark period, negative phase, or eclipse period. In this stage the elementary body disintegrates and gives rise to the immature virus, and azurophilic reticular inclusions are observed microscopically.

The azurophilic reticular inclusions appear only during the first seven days of acute trachoma and after that they are never found. In the first week after onset Prowazek-Halberstaedter bodies are mostly small-sized and in the early stage of inclusion formation, and on the seventh and eighth days large mature Prowazek-Halberstaedter bodies appear in abundance. It is very significant that the azurophilic inclusions disappear and are never found after the seventh day, when numerous large mature Prowazek-Halberstaedter bodies appear.

The disappearance of the azurophilic inclusions after the first week is considered to be due to the differences in the intracellular reaction of the host cells to virus invasion during and after the first seven days; that is, they are due to differences in the metabolic process of the host cells.

The azurophilic inclusions are also demonstrated in inclusion conjunctivitis at the onset; they are found during the first three days of inclusion conjunctivitis in newborns. They are identical morphologically with those of trachoma. Trachoma and inclusion conjunctivitis resemble each other strikingly, not only in the morphologic identity of their Prowazek-Halberstaedter bodies and the azurophilic inclusions but also in their clinical pictures.

Furthermore, it is of much interest that azurophilic inclusions are occasionally demonstrated at the onset of epidemic keratoconjunctivitis, although they are in small number. Morphologically those of trachoma and epidemic keratoconjunctivitis appear to be identical. The presence of azurophilic inclusions in epidemic keratoconjunctivitis

seems to be evidence that the disease is due to a virus. The differential diagnosis between acute trachoma and epidemic keratoconjunctivitis is based on the presence of Prowazek-Halberstaedter bodies in the former.[19]

Ochi[20] reported that inclusion bodies were demonstrated in an acute conjunctivitis which occurred among bathers in pools. The inclusion bodies consist of a reticular structure and their staining reaction is similar to that of the nucleus. Prowazek-Halberstaedter bodies were not found. Occasionally punctate keratitis develops. The inclusion bodies reported by Ochi are considered to resemble azurophilic reticular inclusions morphologically.

It is generally agreed that Prowazek-Halberstaedter bodies constitute intracellular colonies of the virus in various stages of development. The elementary bodies are the morphologic unit of the virus and are seen during the infective stage. They swell to become the initial bodies. As the elementary and initial bodies multiply and increase in number, Prowazek-Halberstaedter bodies grow larger.

Prowazek-Halberstaedter bodies undergo a regular sequence of morphologic development from a small immature form to a large mature form and again to a small immature form in a new host cell. This sequence is considered to represent their growth cycle. The virus has a life cycle from elementary body to initial body and again to elementary body. However, the virus seems to multiply mostly in the sequence from elementary body to elementary body directly.

The following interpretation of the growth cycle of Prowazek-Halberstaedter bodies is offered:

1. A free elementary body penetrates a conjunctival epithelial cell.
2. The elementary body then becomes smaller and develops into an immature virus. In this period the azurophilic reticular inclusions are seen.
3. The immature virus ripens to become the elementary body.
4. The elementary body swells to become an initial body.
5. The initial body then divides to form elementary bodies.
6. The elementary body multiplies and the elementary body stage is reached.
7. The cytoplasm of the cell is entirely replaced by the inclusion mass.
8. The cell ruptures liberating the elementary bodies into the secretion (fig. 7).

The process of multiplication is considered to be a combined action between the invading virus and the host cell. The formation of the matrix around the seat of the virus multiplication is considered to be an intracellular reaction of the host cell to the virus invasion and consists of an accumulation of protoplasmic material. Accordingly, it may be concluded that Prowazek-Halberstaedter bodies are essentially intracellular colonies; that the elementary and initial bodies are the virus itself; that the azurophilic reticular inclusion bodies are the immature virus; and that the polysaccharide matrix and plastin-like substance are reaction products of cell origin.

A significant difference is observed between the relative amounts of polysaccharide matrix to be found in the different stages in the growth process of Prowazek-Halberstaedter bodies. In general, the amount of the matrix increases with growth; the large mature Prowazek-Halberstaedter bodies contain a larger quantity of polysaccharide than the small young bodies. Accordingly the polysaccharide matrix is believed to be produced with multiplication from elementary body to elementary body.

Thygeson[21] stated that glycogen in Prowazek-Halberstaedter bodies may be produced in the multiplication from elementary body to initial body and that Prowazek-Halberstaedter bodies found in trachoma contain a larger amount of glycogen than those in inclusion conjunctivitis. However, from my results it is concluded that the difference in the amount of polysaccharide in Prowazek-Halberstaedter bodies found in

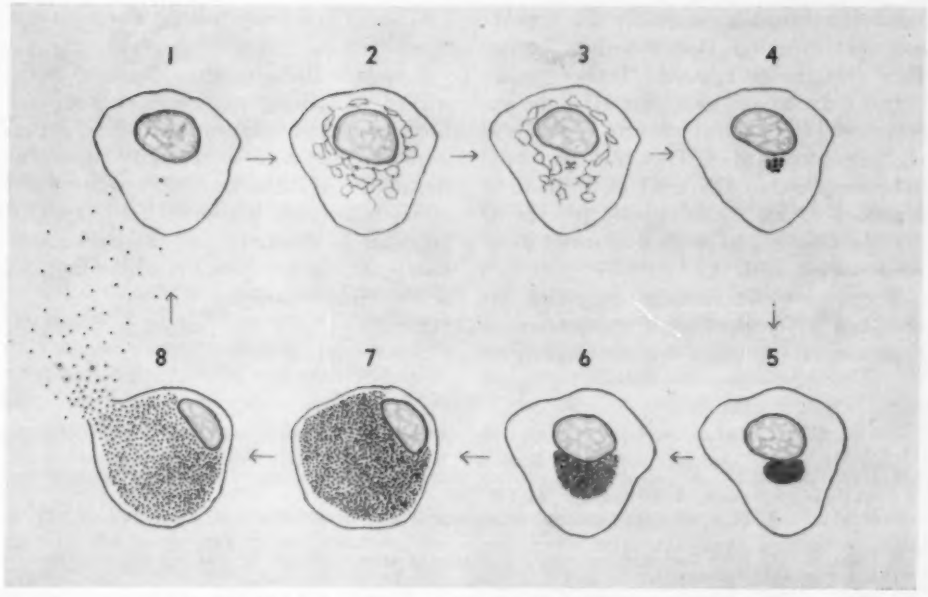

Fig. 7 (Mori). Growth cycle of Prowazek-Halberstaedter body.

1. A free elementary body enters an epithelial cell.
2. The elementary body becomes smaller and develops into an immature virus. In this period azurophilic reticular inclusion bodies are seen.
3. The azurophilic reticular inclusions give rise to a Prowazek-Halberstaedter body consisting of several elementary bodies. As the Prowazek-Halberstaedter body grows larger, the azurophilic inclusions fade and disappear.
4. The elementary body swells to become an initial body.
5. The initial body divides to form the elementary body. A small young Prowazek-Halberstaedter body is seen.
6. The elementary body multiplies and the elementary body stage is reached. A developing intermediate Prowazek-Halberstaedter body is seen.
7. The cytoplasm of the cell is entirely replaced by the inclusion mass. A large mature Prowazek-Halberstaedter body is seen.
8. The cell ruptures liberating the elementary bodies into the secretion.

trachoma and inclusion conjunctivitis is not due to the essential differences in the nature of their respective inclusions, but due to the difference in the stages of their growth; namely, whether the scrapings reveal Prowazek-Halberstaedter bodies of the elementary body type in large numbers or those of the initial body type in large numbers.

The staining by iodine for glycogen has been employed for the demonstration of Prowazek-Halberstaedter bodies.[1, 21–23] However, the bodies present differences in the staining reaction; some are positive, others are negative. The iodine reaction is not absolutely specific and can be said to have little more than a historical interest. Furthermore, goblet cells, when stained with iodine, show a brown-staining mass in the cytoplasm which could be mistaken for Prowazek-Halberstaedter bodies. Accordingly, identification of Prowazek-Halberstaedter bodies must be checked with Giemsa stain.

VII. Summary

Azurophilic reticular inclusion bodies are demonstrated in the early stage of acute trachoma and inclusion conjunctivitis. They are demonstrated in the cytoplasm of the con-

junctival epithelial cells before the appearance of Prowazek-Halberstaedter bodies. They give rise to Prowazek-Halberstaedter body formation and disappear after the appearance of abundant mature Prowazek-Halberstaedter bodies. They are considered to be composed of DNA, which seems to be produced during the metabolic process of the host cells and to be used as materials of virus nucleic acid.

The azurophilic reticular inclusions are occasionally found in small numbers at the beginning of epidemic keratoconjunctivitis. This seems to indicate that the disease is due to a virus.

Prowazek-Halberstaedter bodies were studied morphologically by means of the Giemsa method and various histochemical methods. They seem to constitute intracellular colonies of the virus. The elementary and initial bodies are the virus itself, and the polysaccharide matrix and plastinlike substance are reaction products of the host cell to the virus invasion.

No. 8, Chitose-cho.

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EVISCERATION WITH RETENTION OF THE CORNEA*

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Since the time of the first enucleation, ophthalmic surgeons have tried to replace the eye with some form of prosthesis that would give the patient a natural appearance. They found that, for best results, two things are necessary: the replacement of orbital volume, and the placing of a shell or plastic eye in the socket. However, the problems of fixed stare and the lack of ocular movement have always been the severest handicaps in the use of any sphere within Tenon's capsule, or any other appliance that does not move with the fellow eye and does not fill out the socket.

The best match for an eye is the fellow eye. In the procedure I am about to describe, the volume can be maintained close to the total and the rest can be replaced by a shell, placed as a contact lens type of cover over the front of the eviscerated eye. Over a period of 25 years, I have tried many different methods of enucleation and evisceration. The full plastic implant, I now believe, still gives the most satisfactory appearance, but it is surgically impractical.

The first evisceration I saw was done by Dr. Frank Burch in St. Paul some 25 years ago. The method I am reporting today is quite similar. It has been performed successfully on 95 percent of more than 200 patients. It is a straightforward, logical surgical procedure that can be done in almost every instance without complication and without difficulty.

The two main contraindications for evisceration are: first, the presence of a tumor within the globe; second, the possibility of causing sympathetic ophthalmia, which, as everyone appreciates, would be extremely serious. We have met the complication of tumor within the orbit on two occasions. One of the cases was an old uveitis patient who asked to have her eye eviscerated for appearance's sake, and in doing so we encountered a melanoma, necessitating enucleation of the eye. This patient has given us no complication since that date. We have never encountered a sympathetic ophthalmia, nor have we encountered any situation that remotely resembled it.

The surgical procedure is not a difficult one. An incision is made from the 9- to 3-o'clock positions through the conjunctiva; then, with a cataract knife, the sclera is incised throughout the extent of the above incision, nearly 180 degrees. The incisions are approximately between 8.0 and 10 mm. from the margin of the cornea, anterior to the superior rectus muscle. Picking up the margins of the wound, fixing three or four hemostats, separating the wound, and then, with a forceps wrapped in gauze, removing the content of the orbit is the next procedure, which may be done without difficulty. However, special care must be taken to remove every shred of the uvea to avoid sympathetic ophthalmia. The globe can be everted, and hemorrhage can be stopped by cautery; the inside of the eye is then wiped out with an applicator impregnated with iodine, irrigated with alcohol, and finally with saline. An 18 or 19 polyethylene or KLF sphere is then inserted inside the scleral shell.

Over a period of years we have used two types of balls: a plain polyethylene sphere or a mesh-covered ball. Either one is satisfactory. We have used varieties of mesh-covered balls. I would like to stress at this point that one should not put in too large a ball, as it will stretch the sclera, and, if subsequent hemorrhage should increase the pressure of the eye, the wound may open.

Using a double-armed 3-0 catgut, the

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* Presented at the 92nd annual meeting of the American Ophthalmological Society, Hot Springs, Virginia, June, 1956.

scleral wound is sewn together at the 12-o'clock position. Then, using one arm of this suture and locking the stitches as one goes along, and with one arm of the suture going toward 9-o'clock, the wound is closed to the 9-o'clock position, and then, with the other length, closed to the 3-o'clock, bringing the arm of the suture up through the conjunctiva. The conjunctiva is finally closed, reversing the direction with the same suture and tying the suture together at the 12-o'clock position.

The main problem in evisceration is to replace volume; an 18-mm. sphere is the smallest that should be used in almost every instance, and it is possible to go as high as a 20-mm. ball in an old buphthalmic globe. It is not necessary to place a conformer in the socket; as a matter of fact, it is wiser not to, as one may establish a pressure point, should subsequent edema make the eye very hard.

The lids are sewn together, and the edema is reduced by means of an iced glove or cold compresses. In questionable cases, we give preoperative antibiotics and continue them for several days postsurgically; we have also used antihistaminics such as Chlortrimenton or Pyribenzamine to lower the incidence of edema and reaction.

The reaction is sometimes quite severe. The lower conjunctiva becomes edematous, and the eye becomes quite firm and sometimes painful. The pain is usually controlled by sedatives; sometimes Demerol is necessary. This pain may persist for several weeks, especially if the lid sutures do not hold. At this point, I would like to call attention to the fact that two interrupted sutures are better than one. I should also like to mention that the edema and conjunctival reaction may last as long as a month.

The complications have been those of discomfort, rather than of infection or of extrusion of any of the spheres. The most difficult part of the entire procedure is that of fitting the shell, which must be fitted in the manner of a contact lens; for that reason we have called this type of shell a contact shell. Frequently an impression of the eye and socket is made to insure a perfect fitting. There can be no pressure points on the cornea; otherwise the cornea or sclera may rub through or erode. This is especially likely to happen during the early postsurgical months.

Mucus has not been one of the serious complications of this type of procedure, but, when it occurs, one can put a small hole through the shell similar to the lacril-hole of a contact lens and cleanse the posterior part of the shell with a DeVilbiss spray or similar apparatus. Infection has never been a complication of this procedure.

The advantages of this procedure, as one can see, are numerous. The entire eye does not need to be removed, and the patient is not so seriously traumatized psychologically. The eye is in its proper position in the socket, and has simultaneous movement with its fellow. The extent of the movement is the greatest that one can obtain. In most instances there is little or no drainage; there is practically no sulcus in the upper lid. This procedure can be done in almost 99 percent of all cases, and it should be done as a primary procedure in eyes badly traumatized in industry.

In summary, (1) a simple and direct method of evisceration is described, which can be performed in most cases; (2) the procedure does require an excellent shell-fitter; (3) a lacril-hole may be of some advantage; (4) results in terms of appearance and movement are very good.

David Whitney Building (26).

THE TREATMENT OF OCULAR ALLERGY*

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Prerequisites for the successful management of allergic reactions of the eye are: (1) recognition that an allergy is present; (2) the proper classification of the allergic mechanism involved; and (3) the discovery, if possible, of the sensitizing substance.[1] On many occasions, because ocular allergies often resemble inflammations of nonallergic origin, such as bacterial and viral infections or reactions to direct primary irritants, allergy is not recognized when it is present, or is erroneously diagnosed when it does not exist. Therefore, unless each case is properly evaluated, serious problems in the management of these patients may arise, problems that modern-day therapy may aggravate rather than resolve.

For the understanding and classification of ocular allergies, one must accept the concept that allergic reactions are of three basic varieties: (1) an immediate anaphylactic or atopic (familial allergy) response, occurring a few minutes after antigen exposure, due to pollens, inhalants, animal proteins, or foods; (2) a delayed (24 to 48 hours) response due to products of microbial infection; and (3) a delayed response due to contact allergy from drugs, cosmetics, and other chemical products. All allergic reactions occurring in the eyes, with the exception of vernal conjunctivitis, may be explained by one of these mechanisms. Successful management requires that treatment be based on the particular mechanism involved.

The therapeutic regime in allergy of the eyes should be: if the cause cannot be eliminated, major reliance should be placed on nonspecific measures and drugs. Desensitization is reserved for special instances. An important principle, especially in contact allergies, is the avoidance of any medicament in the treatment, likely to arouse new sensitivities in highly sensitized tissues, not likely to be allergic to these drugs at other times.

STEROIDS

As in other forms of allergy, the corticosteroids have proved of tremendous value in the treatment of ocular allergies, even though their action is both nonspecific and noncurative. However, the abuse of the steroids has in large measure detracted from the great advantages these products offer. Their use in the eyes is not without danger; a fact that many general physicians and pediatricians ignore.

CONTRAINDICATIONS TO TOPICAL USE OF STEROIDS

Contraindications to the local use of steroids for ocular allergies include allergic and irritative reactions, the triggering of infections with the virus of herpes simplex, and the possibility of introducing bacterial infection by means of contaminated solutions. Allergy is rather rare and not serious; neither is irritation (due to the particles in suspensions of the drugs used[2]). The aggravation or causation of herpes simplex infections of the cornea is, of course, a serious matter.

It is now generally accepted that the local use of corticosteroids where infection with the virus of herpes simplex exists usually results in the most serious sequelae due to the rapid extension of the corneal infection in an eye that appears relatively uninflamed due to the antiphlogistic action of the steroids. A less appreciated danger from continued ocular therapy is the actual causation of herpes simplex infection of the cornea by this medicament. This is not rare in our experience and those of others.[3] In all persons prone to the recurrence of herpetic in-

* Presented at the symposium on Ocular Therapy, IV Interim Congress, Pan-American Association of Ophthalmology, April, 1957.

fections in general (such as cold sores), and particularly in those with a previous history of herpes simplex (dendritic) keratitis, routine local use of steroids in the eyes is unwarranted and may be dangerous. The herpes virus present in an inactive state in the tissues of such persons is triggered into activity by the local steroid therapy.

The widespread use of steroids in combination with antibacterial agents has inadvertently accentuated these dangers. Beguiled by the apparently logical basis for these combinations, as promoted by their manufacturers, who cite their broad value against both bacterial infections and allergies, they are used with abandon, not so much by ophthalmologists, but by other physicians, often for long and disastrous periods of time. Since only ophthalmologists are equipped to recognize herpetic infections of the cornea, warnings against the use of these products for such viral infection, now common in the pharmaceutical literature provided, are without any real meaning.

Contamination of ophthalmic solutions by pathogenic bacteria as a cause of serious corneal infection was highlighted by the introduction of commercially prepared ophthalmic cortisone solutions.[4] Due to lack of proper precautions gross infection with Pseudomonas aeruginosa (B. pyocyaneus) occurred. The particular vulnerability of cortisone and its analogues to such contamination became apparent. This led to United States governmental regulations requiring the sterile preparation of all commercial ophthalmic solutions. It must be remembered however, when using corticosteroids, that the danger of secondary infection, through solutions infected *during* usage, still exists, and that proper care must be exercised to avoid this.

Antihistaminics

The basis of antihistamine therapy is, first, that histamine plays a prominent part in anaphylaxis and in certain other forms of allergy, and, second, that the antihistaminics nullify histamine action by combining with the target cell, preventing the absorption of histamine by these cells and, thus, the resultant allergic reaction.

Since histamine plays an important role in the "immediate" form of allergic response, it has a therapeutic indication in both reactions when used systematically, not locally. In patients suffering from seasonal hayfever, for example, if the oral use of antihistaminics is of value, the associated conjunctivitis is often greatly alleviated, even if not completely so. It is unfortunate that the local use of antihistaminics appears to have little, if any, therapeutic value.

Since histamine plays little or no demonstrable role in the "delayed" forms of allergy, one should not expect, nor does one find, antihistaminics to be of value in either contact or microbial allergies. Antihistaminics frequently cause contact allergy.

Outline of treatment of ocular allergies

Allergic conjunctivitis

Atopic conjunctivitis. This is due to pollens, dusts, danders, other inhalants, and foods. Where elimination of the cause cannot be accomplished, treatment should be based as follows: (1) because the reaction is an exudative response with vasodilation, vasoconstrictors, used both locally and systemically, give the most rapid immediate relief; (2) because histamine plays a role in the pathologic physiology, antihistaminics are useful when given systemically; (3) because it is a manifestation of the "immediate" form of allergic response, desensitization is often successful; and (4) blocking agents like the steroids, used locally or systemically, are valuable, but not as dramatically so as the vasoconstrictors. In special instances, adjuvants such as air-conditioning are useful in pollen allergies. In chronic atopic conjunctivitis where there is less vasodilation and edema, less emphasis is placed on vasoconstrictors. If the cause cannot be eliminated, treatment begins with topical steroids. Anti-

histaminics, used orally, are indicated. If necessary and possible, desensitization is attempted by the allergist. In severe cases systemic steroid therapy as well as systemic vasoconstrictors such as ephedrine are useful.

Microbiallergic conjunctivitis. This is due to marked sensitivity to staphylococcal products. The treatment of this entity requires the use of staphylococcal toxoid and autogenous vaccines. Local medicaments are used symptomatically. Potent antibacterial agents are neither indicated nor effective.

Allergic dermatoconjunctivitis. This is the result of medicaments, chemicals, and, sometimes, cosmetics. The best treatment of drug allergy is to eliminate the offending medicament and to use, if necessary, another drug having a similar pharmacologic action. The drug substituted should differ as much as possible chemically from the original excitant, because once sensitization to a drug is evoked, allergies to related drugs are more prone to occur. The drug chosen should also be the least likely to sensitize of all the medicaments available for the purpose, because, when an allergy occurs, many drugs, ordinarily harmless to the patient, may act as allergens. Furthermore, even in the absence of an allergy, if an allergic background or history exists, the choice of the drug initially used should be based on these criteria.

Serious and permanent sequelae have occurred following the indiscriminate use of highly allergenic antibacterial agents. These could have been avoided by the use of other equally useful, but safer, medicaments.

If it is necessary to continue the use of a drug causing contact allergy, the concomitant administration of sufficiently large amounts of corticosteroids or corticotropin (ACTH) systemically is advised. Sometimes the local use of ophthalmic cortisone will suffice, permitting the continuance of the allergenic medicament; however, a definite quantitative dosage factor exists in regard to these hormones and must be kept in mind.

Local steroids are of value in expediting recovery in allergic dermatoconjunctivitis and should be prescribed along with elimination of the offending agent. If necessary, in severe reactions, systemic steroids or ACTH may be given for the short period generally needed for improvement to occur.

Antihistamines, both systemically and locally, have not proved valuable, in my experience, in allergic dermatoconjunctivitis, nor should they, on theoretical basis, be expected to be useful.

Vernal conjunctivitis. The best treatment of this self-limited disease is the use of steroids, at first systemically, then only locally after improvement begins. Local soothing applications such as iced compresses, vasoconstrictors, mild anesthetics, sodium propionate, sodium carbonate, are all useful. Removal of large vegetations by carbon dioxide snow may help. Radiotherapy is rarely indicated and is not without danger.

Allergies of the Eyelids

Urticaria and angio-edema. These generalized "immediate" atopic and anaphylactic reactions are best treated with elimination of the cause, if possible, systemic antihistaminics, and vasoconstrictors. Steroids may be helpful.

Infectious eczematoid dermatitis. This allergic dermatitic reaction to local bacterial infection of the eyelids requires elimination of the cause with antibacterial agents, local steroids for the dermatitis, and desensitization with staphylococcus toxoid and vaccines. The application of silver nitrate to the skin of the eyelids is valuable.

Contact dermatitis of the eyelids. Contact allergy of the eyelids is usually due to drugs, cosmetics, chemicals, or articles of apparel. Drug allergy has been discussed.

The actual incidence of allergy from cosmetics is very low if we consider how extensively they are utilized. On balance their use appears to do much more good than harm. Treatment requires elimination of the offending cosmetic and the use of steroids. Generally, their local application is sufficient;

on occasion, systemic therapy is necessary. Hypoallergenic products may be substituted. Even if these cause allergies, special formulas can be made by the manufacturers so that few allergic ladies need be compelled to lead a bleak and pale existence.

Allergies of the cornea[5]

Atopic reactions. Allergic keratitis due to foods and pollens are relatively rare. Avoidance of the cause, if possible, and the use of steroids are effective. Antihistaminics may be useful. Specific desensitization may be necessary.

Contact reactions. Allergic keratitis from drugs and other contactants are treated like other contact allergies.

Microbiallergic reactions. Keratitis due to endogenous microbial allergy manifests itself as follows: (1) marginal keratitis (staphylococcus), (2) phlyctenular keratitis (tubercle bacillus, staphylococcus), (3) interstitial keratitis (lues, tubercle), and (4) disciform keratitis (herpes-simplex virus).

Marginal keratitis responds to corticosteroids, treatment of the associated conjunctivitis with antibacterial agents, and desensitization with staphylococcus toxoid.

Phlyctenular keratitis responds to steroids, treatment of secondary staphylococcal infection in those patients with allergy to tubercle bacillus products, and the use, if necessary, of toxoid in primary staphylococcal phlyctenulosis.

Interstitial keratitis would appear to be an allergic response to luetic infection. As such, steroids and foreign protein seem more effective than antiluetic therapy, which, indeed, may aggravate the keratitis in a type of Herxheimer reaction.

In disciform keratitis of the classical type, that is, where the epithelium is intact, it is believed by some observers that an allergy to the virus of herpes simplex may override the infectious component. In such instances steroids may be used with great caution. The condition must be distinguished from the chronic geographic type[3] of herpes simplex where infection predominates and steroids may prove disastrous.

Allergies of the sclera

Atopic reactions. Food and inhalant allergies of the sclera are treated like other atopies; the cause is eliminated if possible, local corticosteroids and systemic antihistaminics are used, and specific pollen desensitization occasionally employed.

Microbial allergy. Episcleritis and scleritis appear to arise on the basis of bacterial allergy to the staphylococcus, the streptococcus, and tubercle bacillus. The latter type of allergy appears responsible for sclerosing keratitis as well. Local steroid therapy and specific desensitization with vaccines or toxoids are indicated.

Scleritis in "collagen" diseases. Scleritis developing in gout, rheumatic fever, rheumatoid arthritis, and periarteritis nodosa responds either to specific therapy or the use of steroids, locally and systemically.

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NOTES, CASES, INSTRUMENTS

DIAGNOSIS OF GLIOMATOUS PSEUDO-UVEITIS*

Report of a case

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The extension of a retinoblastoma into ciliary body and iris induces inflammatory signs which are the predominating finding in the clinical picture. There do not exist reliable reports as to the frequency of gliomatous pseudo-uveitis but it seems to be comparatively rare. The world literature in 1926 according to Velhagen included only 26 cases.

The difficulty in the differential diagnosis between endophytic growing gliomas with extension into the anterior uvea and tuberculous and other bacterial inflammations has been repeatedly emphasized (Lagrange, 1901; Dollfus, 1935).

The obvious attempt to clear up the etiology of such processes by biopsy turned out to be quite disastrous. Jung, for instance, observed in a case of pseudo-uveitis after iridectomy, the rapid extraocular spreading of a retinal glioma with a fatal end. The diagnostic puncture of the vitreous body as recommended by Gabriélidès is, therefore, rejected by Dollfus and others. The diagnostic puncture of the anterior chamber, however, should hardly be the reason of an extraocular metastasis of a glioma. If enucleation becomes necessary it should be delayed several days, as Verry proposed.

A clinical examination of the aqueous humor has been performed infrequently to differentiate between uveitis and gliomatous pseudo-uveitis. Only three authors reported positive results:

Hirota (1922) described glioma cells in the whitish-bloody content of the anterior chamber of an eye with obscure symptoms of eye disease.

Salvati (1924) wrote of glioma cells in aqueous humor in a case of retinitislike alterations of the fundus.

Denti (1938) found glioma cells in aqueous humor in a case of a glioma masked by heavy pseudo-uveitic symptoms. Barletta (1930) and later on Thomas (cited by Verrey, 1935) described similar findings in cases of already diagnosed glioma.

To these scanty case reports we add another. This is the case of a six-and-one-half-year-old boy in whom the unilateral eye disease corresponded more to a picture of a tuberculous panuveitis than to a glioma of the retina. The gliomatous etiology of the panuveitis was cleared up by diagnostic puncture of the anterior chamber.

Case report

History. E. F., a six-and-one-half year old boy of German origin had a noncontributory family history. There was a two-to-three month history of repeated inflammation of the left eye.

Ophthalmologic examination. Right eye. Vision was: 5/5 with a refractive error of +1.0D. sph. Intraocular pressure: 20 mm. Hg (Schiøtz). Otherwise the findings were entirely normal.

Left eye. Vision: 1/30. Moderate ciliary injection was present. Corneal epithelium was clear; on the endothelial surface were fine glistening precipitates. In the aqueous humor there were numerous corpuscles of varying size in slow heat motion. At the bottom of the anterior chamber was seen a hypopyon with a convex edge. The iris was studded with rather large irregularly arranged nodules resembling snowflakes (fig. 1). The anterior surface of the lens also showed precipitates, and the deeper layers were coarsely turbid so that visualization of the fundus was difficult. The anterior portion of the vitreous contained corpuscular specks. The inferonasal retina showed a bullous detachment. In the upper half of the retina, sporadic vessels and whitish nodules could be seen. No shadow was seen on transscleral illumination. Intraocular pressure: 45 mm. Hg (Schiøtz).

Pediatric evaluation showed development corresponding to age. Physical examination was within normal limits. Sedimentation rate, 15/36. Blood picture: relative lymphocytosis 50 percent; absolute, 2,800. Moro reaction positive.

Differential diagnosis. The history, laboratory findings, and the alterations in the iris pointed to

* From the University Eye Clinic. Director: Prof. Dr. Rohrschneider.

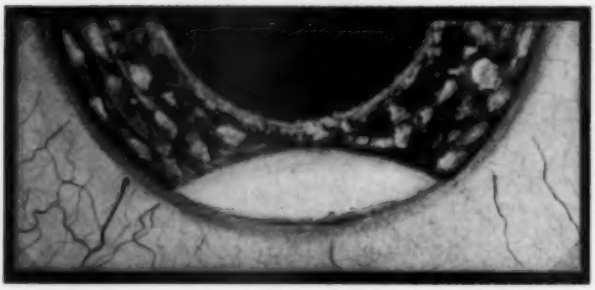

Fig. 1 (Küchle, Remky, and Sattler). Anterior sections of the eye, showing iris nodules, pseudohypopyon, and precipitate.

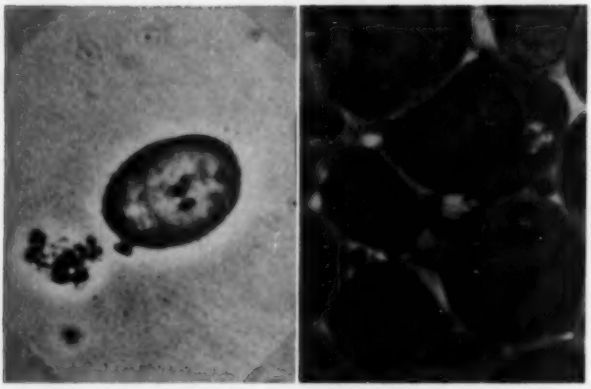

Fig. 2 (Küchle, Remky, and Sattler). (Left) Free tumor cells in aqueous humor. (Right) Degenerated cells from a collection in the aqueous.

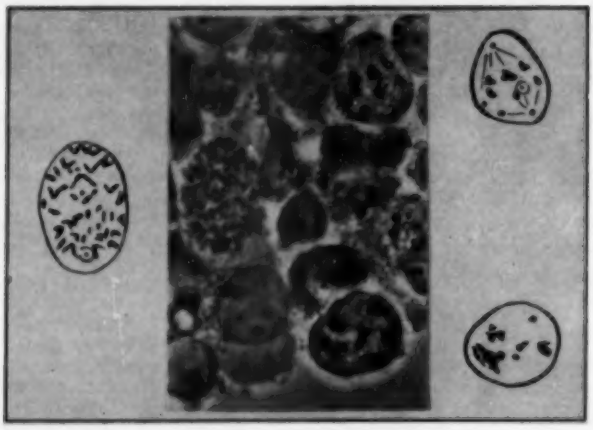

Fig. 3 (Küchle, Remky, and Sattler). Tumor cells in mitosis (metaphase). (Vital preparation of the aqueous.)

the possibility of a tuberculous process. On the other hand, lack of posterior synechias, hypertension, and the properties of the described corpuscles pointed to the possibility of a gliomatous disease.

To resolve the diagnosis, a puncture of the anterior chamber was performed, as is done in all cases of uveitis in our clinic.

Cytologic findings in the aqueous humor. Vital fluochrome-stained preparations were examined in the phase-contrast microscope and in fluorescent dark-field (method of H. Remky). Both methods showed many single cells and cell collections. These were different from the blood and tissue cells ordinarily found in the aqueous humor in inflammatory uveitis. In this case there were large cells

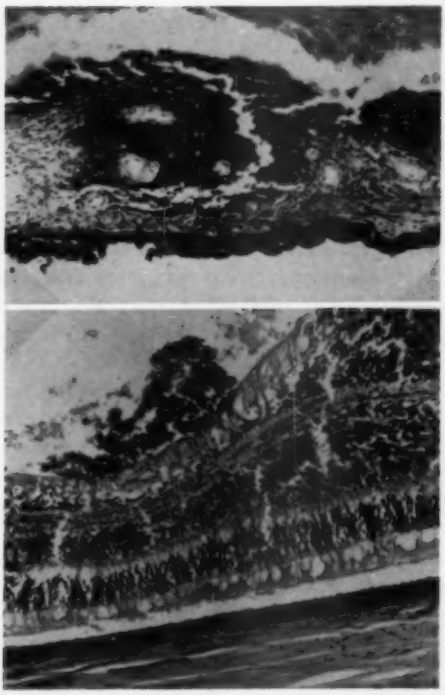

Fig. 4 (Küchle, Remky, and Sattler). (Above) Section through an iris metastasis. (Below) Section through the surface of a retinal metastasis.

(up to 50 microns) with scanty cytoplasma and centrally placed nuclei. The nuclei contained many nucleoli and coarse chromatin granules. The nuclei appeared swollen and, according to their quality of fluorescence, they were probably dead before the examination. On the edge of the cell collections, however, there were numerous mitotic figures, mostly in the metaphase stage, an expression of high cell vitality. The great number and irregular pattern of the chromosomes showed an excess of mitotic activity (figs 2 and 3).

There was no doubt that the cells were of tumor origin and appeared to be malignant. The diagnosis of a gliomatous pseudo-uveitis was proven by the pathologic examination of the enucleated eyeball.

Pathologic findings. Macroscopic examination showed no infiltration of the adnexa, Tenon's capsule, optic nerve, and its coverings. Peculiar whitish dust was seen on the ciliary body. The vitreous showed numerous whitish particles. In the upper nasal quadrant a white tumor mass, about 10-mm. in diameter, was seen. The retina showed numerous whitish nodules with petechias in between.

Histology. The tumor itself showed a typical picture of sheets of cells which consisted almost entirely of chromatin-rich nuclei the greater proportion of which were degenerated. In some areas there was gross necrosis. In the vicinity of the vessels there were many pseudorosettes. Flexner-Winterstein rosettes were scanty and not fully developed. Calcification, also, was only rarely found. The infiltrative nature of the tumor was evident. Scattered over the entire retina were small metastases which infiltrated to the inner reticular layer and even to the choroid. Groups of tumor cells were on the anterior surface of the iris and within the iris stroma. The chamber angles were filled with tumor cells. This was a typical picture of a retinoblastoma —glioma without rosettes (fig. 4).

Summary

A case of pseudo-uveitis in retinoblastoma showing the clinical picture of a panuveitis is reported. The patient had recurrent inflammation and the presence of nodules on the iris, hypopyon, and general symptoms led to the clinical impression of a tuberculous etiology. A diagnostic puncture of the anterior chamber showed the presence of glioma cells; the vital preparation of the aqueous fluid showed degenerated cells and also numerous mitotic figures. The histology of the enucleated eye proved the diagnosis of a retinoblastoma.

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AKINESIA OF THE ORBICULARIS OCULI*

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The advantage of a paralytic orbicularis oculi during a cataract operation and several other types of ocular surgery is obvious to all ophthalmic surgeons. There are, however, several methods of obtaining this paralysis and each technique has its advocates. The common aim in all techniques is to paralyze the facial muscles which may exert pressure on the eyeball and express the ocular contents. The procedures commonly referred to in the literature are those of van Lint,[1] Wright,[2] O'Brien,[3] and, most recently, Atkinson.[4]

The van Lint technique which was described in 1914 advises the infiltration of the terminal fibers of the facial nerve in the orbicularis muscle. The needle is inserted one cm. posterior to the intersection of a horizontal line along the inferior margin of the orbit and a vertical line along the lateral margin of the orbit. The needle is introduced as far as the bone and directed inward and slightly downward into the deep tissues just below the orbital margin. The injection is given as the needle is withdrawn. Through the same opening in the skin the needle is again inserted as far as the bone and directed upward and inward near the orbital margin close to the bone.

In 1923, R. E. Wright devoted much time to dissecting the seventh nerve in a search for the best site to block it. He finally found his best results were obtained from injecting the nerve as it leaves the stylomastoid foramen. In 1933,[5] when reconsidering his techniques which included a modification of van Lint's peripheral block, he stated that O'Brien's method was more satisfactory.

O'Brien in an article on local anesthesia in 1927 presented his modification of van Lint's procedure. He advocated injecting the fibers of the facial nerve just anterior to the tragus of the ear below the posterior portion of the zygomatic process and directly over the condyloid process of the mandible. Inserting the needle straight inward the bony condyloid process is struck at the depth of one cm. As soon as the bone is felt, the injection is begun and, gradually withdrawing, two cc. of solution are injected.

Atkinson,[6] who has presented several excellent articles on local anesthesia, introduced, in 1953, a new technique for akinesia of the orbicularis. It is briefly: The needle is introduced at the lower edge of the zygomatic bone about one cm. posterior to the intersection of a vertical line drawn from the lateral margin of the orbit and a horizontal line along the lower edge of the zygomatic bone. The injection is made posteriorly along the lower edge of the zygomatic bone and upward across the zygomatic arch close to the bone. The index finger of the other hand over the facial artery and vein protects these facial vessels. It also indicates the direction and terminus of the needle point. In 1955[4] Atkinson modified his procedure and advocated injecting at the inferior edge of the zygoma in line with the lateral margin of the orbit. The anesthetic is injected upward across and close to the zygomatic bone at an angle 30 degrees from temporal margin of the orbit.

During a discussion of akinesia in 1948

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* Presented at the meeting of the Pacific Coast Eye, Ear, Nose, and Throat Society, April 11, 1957, Coronado, California.

Atkinson[7] said, "Of the various modifications of the van Lint method of producing paralysis of the orbicularis the simplest and most satisfactory is the one proposed by O'Brien." In the 1953 article, presenting a new technique, Atkinson's first objection to the O'Brien method is that the nerve is often missed. His other objections are paralysis of the lips and lower face and pain at the time of injection or during jaw movements thereafter. These are undoubtedly the chief reasons every operator doesn't use the O'Brien modification. O'Brien's idea of a single injection blocking the main nerve trunks seems more satisfactory than diffuse infiltration with multiple needle thrusts.

At the present time most ophthalmic surgeons doing cataract surgery use either the van Lint or the O'Brien akinesia; that is, they obtain akinesia by blocking the peripheral fibers or a main trunk of the facial nerve. Those who use the van Lint infiltration or Atkinson's modification or a combination of the two do so because, having tried O'Brien's method with repeated failure, they feel that the shortcomings of the van Lint technique are worth the akinesia it produces. Therefore, to reduce the incidence of akinesia failure and eliminate pain from postoperative jaw movements, a few alterations in O'Brien's technique are proposed.

New technique

The site of the injection is localized with the tips of the index and middle finger and no particular attention is given the tragus of the ear or other surface land marks. With the right hand holding the syringe for operations on the right eye, the index finger of the left hand approaching from an inferior position finds the posterior inferior margin of the zygomatic process, and the middle finger the superior posterior margin of the mandible neck. For the left eye the index finger of the left hand approaching from above locates the posterior inferior margin of the zygomatic process and the middle finger the posterior margin of the mandible neck.

The mandible neck is felt between the finger tips. In patients with heavy cheeks—thick in the parotid area—it is impossible to palpate the anterior border of the mandible neck but it is always possible to feel the posterior margin and the posterior portion of the zygomatic process. The patient's mouth is closed. The injection is made between the finger tips directly onto the mandible neck. This site is below as well as anterior to the tragus. The needle point strikes the neck of the mandible approximately 1.0 cm. inferior to the condyle. The needle must strike the bone and be held firmly against it.

The injection consists of seven cc. of two-percent procaine, five cc. of which are injected while the needle is held firmly against the mandible neck and two cc. during slow withdrawal. In patients with thick cheeks more may be used and in those with thin faces less is injected.

The facial nerve injection is the first step of the local anesthesia technique in preparing the patient for cataract extraction. After the elapse of four or five minutes the akinesia is well advanced and, by the time the conjunctival instillations and retrobulbar injection are finished (eight to 10 minutes) the akinesia is complete. Occasionally the seventh-nerve branches to the lower face are blocked but there have been no complaints from the patients. In no case has any paralysis of the facial musculature been present at the 24-hour postoperative dressing. No complaints of pain from jaw movements have been made because the injection is below the mandibular condyle and temperomandibular joint.

Summary

Most cataract surgeons use either the van Lint or O'Brien techniques for akinesia. Failure to block the facial nerve fibers supplying the orbicularis oculi by the O'Brien method is rare if the injection site is slightly altered and the amount of the anesthetic solution is increased.

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ANGLE-CLOSURE GLAUCOMA*

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In clinical practice one is constantly reminded of the ever-present angle-closure glaucoma (narrow-angle glaucoma) in which obstruction to aqueous outflow results from contact of the root of the iris against the trabecular wall. This glaucoma is characterized by periodicity of obstruction varying in severity from that of an acute attack associated with excruciating pain to one in which the attacks are so mild that they may escape the notice of the patient. The discomforting feature is the number of angle-closure glaucoma cases which are mismanaged due to the failure to recognize the presence of this entity, the true mechanism of the angle obstruction, and the necessity of instituting proper therapy in its early stage.

The present case is extremely unique in that there was no history, clinical signs, or apparent histologic evidence of previous attacks of glaucoma. Both eyes were obtained immediately in a good state of preservation following death from a spontaneous perforation of the heart while in the hospital for the treatment of acute glaucoma. One eye demonstrated the anatomic shallowness of the angle characteristic of this type of glaucoma and the other the same shallowness with complete closure of the angle by the root of the iris pressed firmly against the trabecular wall. Despite the failure to effect an opening of the angle with local use of miotics, the intraocular pressure dropped from 80 to 23 mm. Hg (Schiøtz) in less than 24 hours with the use of acetazolamide (Diamox), demonstrating the effectiveness of this drug in decreasing aqueous formation.

In addition to presenting this interesting case which demonstrates the characteristic shallowness of the angles and the mechanism of angle closure, I wish to emphasize the importance of proper study of the angle in all glaucoma cases. During the past 20 years there has been an ever increasing demand for the universal use of the slitlamp and biomicroscope in ophthalmology. This has now become an accepted procedure. It is believed that a routine and careful study of the angle of each glaucoma case with a gonioscope should also become universally accepted. In this way the treatment of angle-closure glaucoma would be placed on a rational basis, and, in many cases, treatment would be started in the early stage before the angle had become permanently obstructed by anterior peripheral synechias and the trabecula damaged by contact with the root of the iris, which occurs during episodes when angle closure prevails.[1]

Report of case

Miss M. H., a white woman, aged 56 years, on April 21, 1955, complained of severe pain, congestion, and loss of vision in the left eye which had been sudden in onset and had existed for two days. The patient denied any previous history of blurred vision, haloes, or pain in either eye. She stated that she had had normal vision and no difficulty with either eye whatsoever.

The right eye appeared normal grossly with 20/20 visual acuity. Slitlamp and biomicroscopic study showed a shallow anterior chamber. The

* This case was presented at the meeting of the American Ophthalmic Pathology Club, Washington, D.C., April, 1957.

cornea was clear and appeared to be normal. Gonioscopic study of the angle revealed a typical shallow angle. Ophthalmoscopic study revealed mild arteriolar sclerosis but no retinopathy. The optic disc appeared to be normal. The tension was 18 mm. Hg (Schiøtz).

The left eye was extremely congested with moderate edema of the lids. The epithelium of the cornea was edematous. The pupil was dilated and fixed to light. The anterior chamber appeared to be more shallow than that of the right. The tension was 80 mm. Hg (Schiøtz). The visual acuity was reduced to light perception. The cornea was partially cleared with glycerine solution sufficiently to permit study of the interior of the eye. Slitlamp and biomicroscopic study revealed some edema of the stroma but no evidence of an aqueous beam, cells, or keratic percipitates. There was no evidence of old or fresh posterior synechias. The lens was clear. Gonioscopic study showed a completely blocked angle. Ophthalmoscopic study revealed clear vitreous, mild arteriolar sclerosis, but no retinopathy. The disc appeared to be normal.

While in the office the patient was given 500 mg. of Diamox intramuscularly and two-percent pilocarpine solution was instilled at frequent intervals. The patient was admitted to Good Samaritan Hospital where 250 mg. of Diamox was given by mouth every four hours. The patient was sedated with morphine and then placed on frequent instillations of eserine ointment (0.25 percent). The following morning the intraocular pressure was 23 mm. Hg. The pupil was still fixed and dilated and the angle appeared to be obstructed. Diamox was continued and surgery advised. On the following day the patient suddenly died due to spontaneous perforation of the heart.

PATHOLOGY

Right eye. (fig. 1). The cornea measured 11 mm.

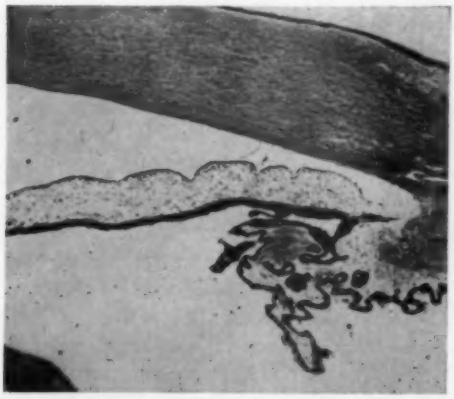

Fig. 1 (Reeh). Low magnification, showing anatomically shallow chamber which is open and functioning.

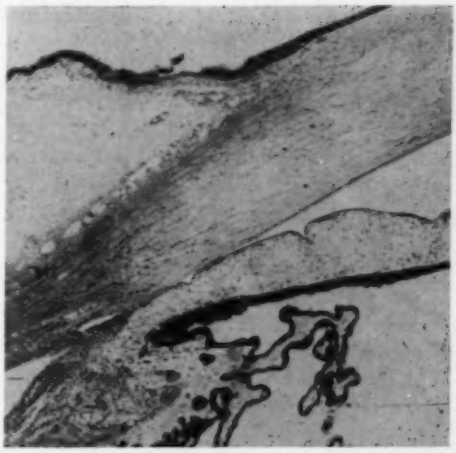

Fig. 2 (Reeh). Low magnification, showing anatomically shallow angle with complete closure by iris against the trabecular wall.

horizontally and 10 mm. vertically. The filtration angle was extremely shallow, chinklike in appearance, with a tendency to convexity of the iris in the periphery. The optic disc and nerve appeared to be normal. There was no evidence of anterior peripheral synechias.

Left eye. (fig. 2). The cornea measured 11 mm. horizontally and 10 mm. vertically. There was marked congestion of the episcleral and limbal vessels. The angle was completely obstructed by the base of the iris which was thrust firmly against the trabecular wall. There was evidence of necrosis of the stroma and sphincter muscle suggesting disturbance of circulation of the iris due to marked elevation of the intraocular pressure. The optic disc and nerve appeared to be normal.

COMMENT

The corneas were slightly smaller than normal. This was considered significant in view of Barkan's[2] observation, "It may be that diminution in the size of the cornea also encourages shallowing of the chamber." These two eyes demonstrated the characteristic anatomic shallowness of the filtration angle, one eye having an open angle and functioning with normal intraocular pressure; the other had a similar angle which was completely obstructed by the base of the iris pressed firmly against the trabecular wall, resulting in marked elevation of the intraocular

pressure and manifesting the symptoms of acute glaucoma.

Attention is invited to the extreme importance of a thorough gonioscopic study of each case of glaucoma so that evaluation can be made on a rational basis and proper therapy begun at once. Almost without exception angle-closure glaucoma requires surgery, usually performed as a peripheral iridectomy with immediate firm closure of the wound. When performed early, this prevents the continued development of anterior peripheral synechias. The addition of Diamox therapy to local use of miotics is even more serious, merely postponing the day of reckoning.

A thorough study of each case of glaucoma, including routine gonioscopy, would aid considerably in correcting the present state of affairs. This was recently called to our attention emphatically by Chandler[3] in a discussion of the use and misuse of Diamox. The failure to understand and appreciate the mechanism by which the angle is obstructed in this type of glaucoma and the unfortunate tendency for the formation of anterior peripheral synechias and sclerosis of the trabecula, resulting in an ever-increasing loss of angle function and a tendency to a rise in the "base tension,"[4] have resulted in many cases of "glaucoma cripples" encountered today.

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and
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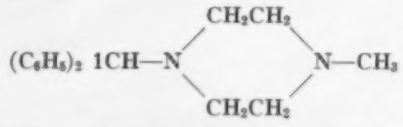
Kansas City, Kansas

The problem of nausea and vomiting following cataract surgery is a most vexing one. It has been variously estimated as being negligible, or to occur in 40 percent of the cases.[1] Nausea and vomiting following cataract surgery is particularly undesirable, as it may be the precipitating factor in a wound rupture, prolapse of the iris, or the occasional loss of ocular contents.[2]

Various drugs have been recommended by Atkinson,[3] such as diphenhydramine (Dramamine®), promethazine (Phenergan®), and chloropromazine (Thorazine®) hydrochloride, to reduce the incidence of nausea and vomiting following intraocular operations.

The following report concerns the use of Marezine®, a brand of cyclizine hydrochloride for the control of postoperative nausea and vomiting. Cyclizine chemically is N-benzhydryl-N-methyl piperazine monohydrochloride with the following structural formula.



Cyclizine is a white crystalline powder readily soluble in isotonic saline solution. Cyclizine possesses an atropinelike and antihistaminiclike action. It appears to act specifically on the parasympathetic ganglia, as the action of injected acetylcholine on the parasympathetic nerve ending is unchanged.[4] Didier et al.[5] have found no demonstrable

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TABLE 1

NAUSEA AND VOMITING FOLLOWING CATARACT SURGERY

	Total No. of Cases	Males	Females	Nausea and Vomiting	Percent
	373	161 (10)	212 (28)	38	10.18
Premedication	218	94 (7)	124 (23)	30	13.71
Premedication with Cyclizine	155	67 (3)	88 (5)	8	5.16

( ) No. of cases vomiting
$X^2 = 6.41$ $P < 0.02$

side-effects following the use of cyclizine when compared with currently used drugs for control of nausea and vomiting.

The technique for anesthesia and akinesia for cataract surgery needs no elaboration. The preanesthetic medication is important since nausea and vomiting may occur following the use of the opiates. The ideal state of sedation is obtained when the patient is amnesic and mentally co-operative, with psychic sedation to obtain a feeling of euphoria.

Of the analgesics available, meperidine hydrochloride (Demerol®) is preferable. Demerol has potent analgesic properties and has a mild sedative action. Respiratory depression is minimal. Demerol possesses an antispasmolytic effect which reduces the incidence of nausea and vomiting when compared with morphine sulfate.

This study confined itself to an evaluation of postoperative nausea and vomiting following cataract surgery with and without the use of cyclizine in the preoperative preparation of the patient. The same premedication was given to all patients. This consisted of meperidine (50 gm.) with pentobarbital (100 mg.) one hour before surgery. The control group received only the above medication. The cyclizine group received, in addition to the above, 50 mg. of the drug intramuscularly, one hour before surgery. The incidence of nausea and vomiting was evaluated for the first 24 hours postoperative. The anesthetic used was tetracaine hydrochloride (Pontocaine®) 0.5 percent solution.

In this series, 373 patients had a cataract operation. There were 161 and 212 females. Nausea and vomiting occurred in 38 patients, 10 males and 28 females. The overall incidence of nausea and vomiting was 10.18 percent (Table 1).

Premedication only was given to 218 patients, 94 males and 124 females. Nausea and vomiting occurred in 30 cases, seven males and 23 females. The incidence of nausea and vomiting was 13.76 percent.

In addition to the premedication, 155 patients received cyclizine 50 mg. before surgery. In this group there were 67 males and 88 females. Nausea and vomiting occurred in eight patients, three males and five females. The percentage of patients with nausea and vomiting was 5.16 percent.

To determine whether or not this percentage decrease was significant, the data were submitted to Alex Sweet, Ph.D., for statistical analysis. The method of the "chi-square" test was used. He reported that the $X^2 = 6.41$ with a P of < 0.02. His conclusion was that "there is a reliable difference between the Marezine group and the control group in incidence of nausea and vomiting. The obtained difference between the two groups in incidence of nausea and vomiting could have been obtained by random sampling fluctuation only less than two times in a hundred."

SUMMARY

Cyclizine lactate (Marezine®) significantly reduced the incidence of nausea and vomiting when used before cataract surgery under local anesthesia.

University of Kansas
Medical Center (12).

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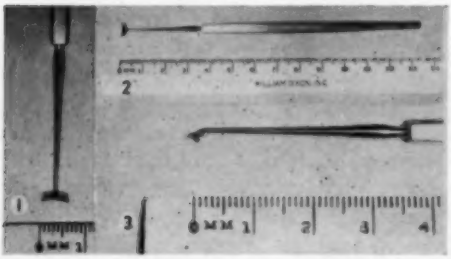
A CORNEAL DEBRIDER

John Sauer, M.D.
New York

Since the methods and instruments for debriding corneal epithelium vary with the operator, it was felt that an attempt should be made to devise a debrider which would have uniform applicability, relative safety, and ease of handling. On questioning one finds that the preference runs from cotton-tipped applicators, to chalazion curettes, to cataract knives, to Took knives, to Gill spoons, and so forth. The preferred radius of curvature of the anterior corneal surface varies according to the observer from 7.7 to 8.4 mm.; the diameter from 11.0 to 12.5 mm.



Figs. 1, 2, and 3 (Sauer). The corneal debrider.

With these requirements the instrument herein described was devised, used and found satisfactory. An arc eight-mm. long with a circle seven mm. in diameter (fig. 1) was attached to a handle (fig. 2) at approximately a 45-degree angle (fig. 3). The flat surface of the debrider is one-mm. wide and on the inside (fig. 1). The instrument is dull and made of stainless steel. The arc can be of varying lengths. However, at present the eight-mm. arc has been found satisfactory.

After the instillation of topical anesthesia, adequate staining with fluorescein, satisfactory exposure and illumination, the instrument is applied to the cornea and with a to-and-fro motion the epithelium is debrided to the desired depth. One may vary the pressure on the cornea. The eyes are then patched after instillation of desired medication.

30 East 40th Street (16).

Acknowledgment

This instrument was made by V. Mueller & Co., Chicago, and I wish to thank Mr. Mertz for his patient and helpful co-operation.

SOCIETY PROCEEDINGS

Edited by DONALD J. LYLE, M.D.

COLLEGE OF PHYSICIANS OF PHILADELPHIA

SECTION ON OPHTHALMOLOGY

March 21, 1957

ISAAC S. TASSMAN, M.D., *Chairman*

BILATERAL SIXTH-NERVE PARESIS

DR. E. HOWARD BEDROSSIAN discussed the differential diagnosis of divergence paralysis, including the symptoms, etiology, and treatment.

The importance of differentiating bilateral sixth-nerve paresis from divergence paralysis was considered, with special reference being made to measuring the fields of fixation on a perimeter, and observing the presence of muscle paretic nystagmus on end gaze.

In reviewing the literature, it was shown that only one case was recorded in which resection of both lateral rectus muscles was done to correct this condition. The present paper shows the effect on improving abduction following resection of both lateral rectus muscles in one case, and following unilateral resection of the lateral rectus muscle in the second case. It was emphasized that proper diagnosis be made, then thorough investigation for neurologic disease be made. If the condition is stationary and nonprogressive, and organic disease is not present, then muscle surgery may be performed to improve abduction.

Two cases were presented, one in which unilateral surgery was performed with good but inadequate results, and the second case in which bilateral surgery was performed with an excellent result, including the pre- and postoperative findings with fields of fixation.

Discussion. DR. WILLIAM E. KREWSON: There is no doubt that many of the cases reported in the literature as paralysis of divergence are actually bilateral abducens palsies of very slight degree, as Dr. Bedrossian has indicated. The majority of cases that have been followed have progressed to a definite paresis of one or both lateral recti and, in some cases coming to autopsy, lesions have been found in the midline between the sixth nuclei. While apparently a disease entity, it may be that paralysis of divergence is a transient phase, or intermittent stage, in the development of typical bilateral abducens paralysis of nuclear origin. I think it is of interest that no cases of paralysis of divergence have been reported in children, so far as I am aware.

We are indebted to Dr. Bedrossian for pointing out the fact that the differential diagnosis of these two conditions frequently is more difficult. We are dependent on the refinements of examination which he has emphasized, especially carefully determined fixation fields, and also diplopia fields taken for various horopters, that is, at different instances. In regard to diagnosis, it is a sad commentary that for a long time nothing very new has been added to our diagnostic armentarium except electromyography. However, this aid apparently is not of much help in this type of case, as far as I can determine from the work of Dr. Breiner. In paralysis of divergence, I understand there may be decreased firing of electrical impulses in the lateral recti on attempted divergence, but also in minimal palsies of these same muscles, the electromyographic pattern may be indistinguishable from the normal. Hence, we must continue to rely mainly on good clinical observation and judgment.

DR. FRANCIS H. ADLER: Dr. Bedrossian started his paper by giving an excellent and thorough definition of the features of divergence paralysis, and with this I am in hearty agreement. The feature he emphasized in this

definition was the difference in the diplopia fields in divergence paralysis and in bilateral sixth-nerve paralysis. In divergence paralysis the diplopia increases with distance, but the angular deviation remains the same when one carries the test object at any one distance in the radius of curvature of a circle from the patient to the right or left. In other words, in divergence paralysis the patient has an angular separation of his images at 20 feet, which remains the same regardless of whether the object is situated in the straight-ahead position, or is carried in the radius of curvature of 20 feet in a circle to the patient's right or left. That is the sine qua non for the diagnosis of divergence paralysis. It is the very essence of the whole picture.

In a sixth-nerve paralysis, no matter how minimal it is, the diagnosis depends on the fact that the diplopia increases in the field of action of the paralyzed muscle; that is, in a bilateral sixth-nerve paralysis there should be no diplopia in the primary position, but an increasing homonymous diplopia when the object is carried to the right or to the left. On this basis it should be easy to make a differentiation between a divergence palsy and a bilateral sixth-nerve paralysis.

Now, in Dr. Bedrossian's cases, he avoids telling us anything about the diplopia field. He lays emphasis on the fixation pattern alone. How can one make a diagnosis on the basis of this evidence? Dr. Bedrossian failed to mention a significant feature which was mentioned by Dr. Krewson and frequently has been emphasized in our literature, and that is that in the vast majority of cases of divergence paralysis a unilateral sixth-nerve palsy frequently occurs at a late stage. This is to be expected, since the lesion which starts in the midline and gives rise to a divergence paralysis in this situation eventually spreads to one or both sides, and the patient ends up with a unilateral or bilateral sixth-nerve palsy. Without seeing his patient, it would be quite unfair for me to claim that this is so, I would at least suggest that Dr. Bedrossian change his title to "Cases of divergence paralysis which eventuated in bilateral sixth-nerve paralysis."

Dr. E. Howard Bedrossian: The measurements which I showed with the fixation fields, in Figures 2 and 3, are the red-glass diplopia fields. It can be seen that they are quite comitant on right and left gaze, which would suggest a divergence paralysis. I was trying to point out that, in a minimal bilateral sixth-nerve paresis, the diplopia fields may appear to be the same on right and left gaze, and thus simulate the findings in divergence paralysis. In such a case, the examiner should then look for a muscle paretic nystagmus on extreme abduction. If he finds a nystagmus, then he should perform a fixation field. The fixation field is a more accurate measurement of abduction ability, and will therefore show a minimal defect which the examiner will frequently not be able to observe grossly. If the fixation field shows an impairment in abduction, then a diagnosis of minimal paresis of the sixth nerve can be made.

Dr. Francis H. Adler: Could you make a diagnosis of sixth-nerve palsy with a diplopia field that did not increase in the direction of action of the palsied muscle?

Dr. E. Howard Bedrossian: Theoretically one should not; however, if one finds nystagmus on abduction, a muscle paretic nystagmus should be suspected and abduction then be measured on a perimeter. It is my feeling that abduction measurements on the perimeter would be more accurate than a diplopia field, in a borderline case. We know that cover test measurements may vary from zero to five diopters clinically, and also the fusion factor may alter the red-glass diplopia measurements. Therefore, in minimal cases such as these, the fields of fixation should be an important differentiating feature.

There have not been enough cases reported in the literature, and those few cases which have been reported have not had accurate fixation fields performed. For this reason, I am asking that more isolated cases

be reported with careful studies, so that further information and results may be obtained.

William E. Krewson, 3rd,
Clerk.

NEW YORK SOCIETY FOR CLINICAL OPHTHALMOLOGY

February 4, 1957

Dr. Max Chamlin, *President*

Double perforating intraocular foreign body

Dr. Victor Goodside presented the case of a 22-year-old man who was struck in the right eye by a glass spicule in April, 1951, while hammering at a broken auto door window. A corneal perforation as well as a lens laceration were noted, followed by swelling of the traumatic cataract and intraocular hypertension. The lens was extracted. When the pupillary area had cleared, a wound of exit one disc diameter in size and five to six disc diameters temporal to the optic nerve in the 9:30-o'clock meridian was found in the retina. The patient had an uneventful postoperative course. Five years later vision, with correction, of the eye was 20/60, and the fundus appeared normal aside from the residual scar of the exit wound. No retinal detachment was in evidence.

Michaelson's differentiation between the transvitreal and tangential type of injury is considered worth making since the pathogenesis of subsequent retinal detachment is different in each case. In the former the detachment occurs at a site removed from the injury, being brought about by a contusion effect, while in the latter excessive scar tissue formation pulls on the retina tearing it.

Discussion. Dr. Posner commented that it is interesting to know whether a posterior detachment of the vitreous had occurred and that one would not expect a retinal detachment if a vitreous detachment was present.

Dr. Benjamin Friedman said that, if a foreign body penetrates through an avascular zone and produces a subconjunctival hemorrhage, it is presumptive evidence that the bleeding comes as a result of a double perforation. The distinction between a single and double perforation in the case of magnetic foreign bodies is extremely important in the surgical treatment. It is well to remember that the injection of air into Tenon's capsule with stereoscopic radiography will often be of great value in deciding whether the foreign body lies inside or outside the eye.

Iridoschisis and glaucoma

Dr. Adolph Posner and Dr. George Gorin said that iridoschisis, or splitting of the iris, denotes detachment of the anterior leaf of iris stroma from the posterior leaf and pigment epithelial layer. No satisfactory explanation of the pathogenesis has been presented. The association with glaucoma has been noted in several instances. No cause and effect relationship was recognized, except for McCulloch who attributed the glaucoma to hypersecretion of aqueous.

The stroma of the iris is composed of two leaves, anterior and posterior. The anterior leaf begins at the collarette and ends at the root of the iris. The root is the thinnest portion of the iris. As a result of progressive involution, defects or crypts are formed in the anterior leaf. The crypts are present mainly in two areas, in the pupillary region and near the root. The crypts communicate with a potential space between the two leaves of the stroma, the space of Fuchs. This space is poorly developed in the majority of eyes. In some cases, however, aqueous may penetrate into this potential space, widen it, and balloon the anterior leaf of the iris forward. In an eye with a shallow chamber and narrow angle, the forward bulging, doughnut-shaped anterior leaf of the iris may produce angle-closure glaucoma, illustrated by Case 1.

M. F., a 56-year-old woman, had bilateral iridoschisis with recurrent attacks of bilateral angle-closure glaucoma. The iris assumed a doughnut-shaped appearance due to ballooning forward of the anterior leaf of the iris. In the lower part of each iris, a defect was present in the anterior leaf, exposing the pigment epithelium. Loose strands of stroma along the margins of the defect waved freely in the aqueous. The patient suffered recurrent attacks of acute glaucoma in each eye. The angle in the right eye was found to be completely closed during an acute attack. Miotics normalized the tension. The separation and ballooning forward of the anterior leaf of the stroma was probably a congenital anomaly and predisposed the eye to angle-closure glaucoma. The formation of holes in the iris stroma on the other hand is a result of acute attacks of glaucoma.

Cases 2 and 3 differed from Case 1 in that iridoschisis was limited to one sector. Here the iridoschisis was secondary to an acute congestive attack of angle-closure glaucoma. During the attack some of the iris arteries, branches of the greater arterial circle, were compressed by the elevated pressure, producing ischemia of corresponding iris sectors followed by necrosis. This strangulation of iris tissue resulted in release of histaminelike substances and these produced the inflammatory symptoms characteristic of acute glaucoma.

In Case 2, that of Mrs. O. G., aged 80 years, examined four days after onset of left angle-closure glaucoma, the tension was 80 mm. Hg, the pupil six mm. in diameter, the cornea steamy, and an intumescent cataract was present. In the inferior sector between the 5- and 6-o'clock positions, the stroma was in contact with cornea and was detached from the iris periphery exposing the deeper layers of stroma and pigment epithelium. Tension was reduced with Diamox, Floropryl, and pilocarpine to normal after 24 hours and on the following day an iridectomy was performed.

Even on the day prior to iridectomy, the anterior leaf of iris stroma was seen to disintegrate into bits of structureless shreds which floated in the aqueous. The more resistant radial fibers, one end still attached to the collarette, waved gently in the aqueous with their club-shaped necrotic free ends. The necrotic material disappeared within three weeks, but the loose fibers of iris stroma have persisted.

Case 3 followed a pattern similar to the second: angle-closure glaucoma and iridectomy in one eye. In the lower nasal quadrant, the anterior leaf of stroma was detached from the iris at the collarette, forming an apronlike membrane attached peripherally to the iris with free edges floating in the anterior chamber.

In summary, two varieties of iridoschisis may be distinguished. The first is a more or less complete over-all separation of the anterior from the posterior leaf of iris stroma. This may be a congenital anomaly. This predisposes to angle-closure glaucoma, especially in the case of a previously shallow chamber. The second type of iridoschisis takes the form of a sector-shaped detachment of the anterior leaf of the iris stroma, the result of angle-closure glaucoma.

Discussion. DR. LEVITT questioned whether iridoschisis and glaucoma could have been coincidental, and also whether iridoschisis might result from trauma.

DR. POSNER replied that he believed there was a causal relationship between iridoschisis and glaucoma in at least two of the three cases cited. He did not see any convincing relationship between iridoschisis and trauma.

CAT-SCRATCH DISEASE

DR. JESSE M. LEVITT reviewed the clinical features of the general disease: a cat scratch causing a trivial skin lesion followed in a few days or weeks by gross enlargement of the regional lymph glands and mild constitutional symptoms such as low-grade fever and general malaise. The glands may suppurate. The disease is self-limited and unaffected by

any known therapy. A positive skin test made with antigen prepared from purulent glandular material or gland tissue from a patient with the disease is specific and essential for diagnosis.

Reported was the case of a 34-year-old woman who observed a small "lump" on left side of her face in front of the ear on October 15, 1956. On October 22nd her left eye became irritated and itchy. She had a slight fever. She had constant exposure to a cat at home but no specific scratch history. The first eye examination on October 31st, 16 days after onset, disclosed, along with a gross enlargement of the preauricular gland and palpable submaxillary and cervical glands, a slight left ptosis, a white globe, and, on eversion of the upper lid, a congested edematous conjunctiva with small nodular elevations with one ulceration.

Biopsy of the involved conjunctiva showed an ulcerative granulomatous lesion consistent with Parinaud's conjunctivitis. No organisms were observed in the microscopic sections. Conjunctival smears, scrapings, and cultures were negative. Wassermann, agglutination test for tularemia, tuberculin test, Frei test, and all other examinations were negative.

The conjunctiva healed entirely by November 15th and the enlarged glands were no longer palpable on December 15th. Positive skin tests with cat-scratch antigen obtained from two different sources supported the diagnosis of cat-scratch disease. Control tests on the patient's husband were negative.

The ocular manifestation of cat-scratch disease takes the form of Parinaud's syndrome. Cat-scratch disease may prove to be a common cause of this symptom complex, along with leptothricosis, tularemia, tuberculosis and so forth. It is possible that some previously reported cases ascribed to mycotic infection were actually cat-scratch disease.

Retinitis pigmentosa, acanthrocytosis, and neuromuscular disease

Dr. Abraham L. Kornzweig and Dr. Frank E. Bassen reported the third case of a rare hereditary disorder characterized by early coeliac disease, progressive ataxic neuropathy, and a peculiar malformation of the red blood cells. Two of the cases reported were in brother and sister; the parents were first cousins. In the third case, the parents were second cousins, so it is believed that consanguinity plays an important role in the development of this unusual condition. The trait probably occurs as a recessive in certain families and manifests itself with consanguinity. The development and course have been remarkably similar in all cases with the important exception, however, that there were no retinal changes in the case reported by Singer et al. In the brother and sister, retinitis pigmentosa occurred, without macular involvement in the boy and with macular degeneration in the girl.

The neurologic signs and symptoms appeared rather late in all the cases and Singer et al. considered the possibility of it being a sequela of the coeliac syndrome. However, we concur with their opinion that the neurologic disorder belongs to the group of hereditary ataxias. The red cell abnormality, which is striking, evidently is an inherent part of the over-all picture. The case herein reported has not been studied in detail hematologically, but the red cell abnormality appeared identical to the other cases described. In the two previously reported cases nothing was found that contributed to our understanding of the malformations of the red cells.

If reports of cases of this type are any indication of the prevalence of this disorder, it must be exceedingly uncommon. The prerequisites of consanguinity plus the presence of the traits in both parents could explain why this condition is so rarely seen. Whether other hereditary ataxic neuropathies, as mentioned by Portier and associates, with or without the hematologic changes, are related, cannot be stated. Close attention to the appearance of the blood smear in related cases of ataxia or retinitis pigmentosa may bring more cases to the fore.

Allergic swelling of lens with transient myopia

Dr. Lewis Schachne described a case of sudden myopia in a young woman. It was accompanied by an increase of intraocular pressure, presumably due to swelling of the lens causing encroachment of the angle of the anterior chamber, for the anterior chamber was seen to widen perceptibly at termination of the episode. Since there had been a previous angioneurotic edema of the face in this patient that had responded to antihistamines, pyrabenzamine was prescribed, with dramatic cure of five diopters of myopia. Several similar cases from the literature were discussed.

Comments from those present concerned mainly the nature of angioneurotic edema and the type of swelling to be found in the lens which is completely avascular. It was felt that angioneurotic edema is but one type of allergic (antigen-antibody) response and that swelling of the lens was another type. Others questioned whether swelling of the lens could ever be considered allergic.

Jessie M. Levitt,
Recording Secretary.

PITTSBURGH OPHTHALMOLOGIC SOCIETY

January 21, 1957

Dr. William Weisner, *presiding*

Selection of operation for glaucoma

Dr. Jay G. Linn, Jr., discussed the surgical treatment of glaucoma from the point of view of the proper selection of an operation and the complete examination of the patient prior to surgery. The preliminary studies included the recording of pressure and vision on several occasions, repeated perimetry, gonioscopy, biomicroscopy, ophthalmoscopy, and special tests, including tonography, when indicated.

The basic types of glaucoma operations were described without discussing specific techniques. The specific operation recommended for each type of glaucoma was that which, by its mode of action, was most likely to rectify the abnormal pathology and physiology responsible for the elevated intraocular pressure. Primary and secondary glaucoma were not discussed as specific entities but the management of all types of both conditions were discussed.

Discussion. Dr. Rohm: What is your attitude toward the use of peripheral iridectomies in the fellow eye?

Dr. Linn stated that in his series of cases of acute glaucoma, which were relieved by iridectomy, 40 percent developed an acute episode in the other eye. He, therefore, suggested peripheral iridectomy as described by Chandler.

Dr. Weiser: What procedure would be followed if the base pressure remained between 28 and 30 mm. Hg in the absence of field changes and visual changes?

Dr. Linn stated that, if it were narrow-angle glaucoma, he would advise operation; if it were open-angle, he might delay but would probably advise operation anyway.

Dr. Thorpe suggested that surgery occasionally converts a wide-angle to a narrow-angle glaucoma by way of peripheral synechias. He stressed maintaining a full anterior chamber. He further stated, in doing an iridectomy, to make certain that the iridectomy is basal because at times the root becomes plastered to the corneal surface. In commenting on so-called low-tension glaucoma, he suggested that a 24-hour curve be plotted; many of these cases would show a rise in pressure.

Dr. Ryan: In a malignant glaucoma would Diamox or a posterior sclerotomy be used?

Dr. Linn stated that a posterior sclerotomy with an air injection would work early. He further stated that in a true flat chamber, the lens would require removal.

Sol Goldberg,
Recording Secretary.

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NONPARALYTIC SQUINT*

Phylogenetic transference of the eyes from a lateral to a frontal position has given primates the advantages of binocular vision. But this depends on so delicate a co-ordinating mechanism that breakdown in development is common. The incidence of squint in school children is high and increasing. In Aberdeen before the late war there was one squinting child in every 30 school entrants; in late years there has been one in every 13.[1]

The binocular mechanism in a child (as in phylogeny) develops late.

At birth the fixation reflex is present but weak; most babies will fix a strong light monocularly for a moment, and some binocularly; otherwise eye

*Reprinted with permission from The Lancet, August 3, 1957, pages 226 and 227.

movements are independent and unco-ordinated. By five to six weeks of age the conjugate fixation reflex is established, and a child will follow a light over a short range. By about three months objects of interest are voluntarily fixed and the beginning of co-ordination of eye and hand movements can be seen. Fully co-ordinated disjunctive movements (convergence and divergence) and conjugate movements do not appear until about six months. From six months till three to four years binocular vision is strengthened by use, and by five to eight years the reflexes have come almost to resemble unconditioned reflexes and, in the absence of disease, will remain so for the rest of life.

The development of such a conditioned reflex may be interfered with at many stages. Each of the 12 extraocular muscles must function normally, and their individual actions must be co-ordinated centrally. The optical systems must form, by a similar accommodative effort in each eye, a clear image at each macula, and there must be co-ordination of accommodation with movement to allow binocular vision for both distant and near objects. Conduction from retinas to occipital cortex must be efficient and central fusion must form one concept from the two peripheral images. Defects in any of these or maldevelopment of the reflexes may cause a squint (commonly convergent) and diplopia, which a child avoids by suppressing one image. If treatment is given soon, as much binocular vision as had already developed may be re-established, but there will be no further development unless the child is under three or four years of age.

Many children with obvious obstacles to development of binocular vision manage to weather the formative years safely, while others with minimal defects break down. In a controlled statistical investigation in Aberdeen, MacQueen and Sutherland[1] showed that a great many children with squint come from small, grossly overcrowded houses. The association was thought to be direct.

"It is not a case simply of overcrowding and squint both being sequels to poverty (for the weights of squinting children do not differ materially from those of controls), or of overcrowding and squint both being evidences of parental 'fecklessness' (for standards of parental care are very little worse in the squinting group than in the controls)."

MacQueen and Sutherland suggest that, if overcrowding is important, this explains why squint is more prevalent in Scotland than in England; and the recent rise in the incidence of squint can be accounted for by higher birth rates in 1946 to 1948, which led to increased overcrowding. There may also be an inherited factor, for in some 40 percent of cases there is a family history of squint, and anomalies have been found in the extraocular muscles.[2-4]

We cannot yet prevent squint but advances have been made in treatment. Of the many who have contributed to current views, probably the greatest was Louis Emile Javal (1839-1907) who, rejecting the idea that the muscles were primarily at fault, suggested that squint was essentially an anomaly of binocular vision and introduced treatment by orthoptic exercises with the stereoscope. The present-day treatment of squint, which has largely grown from Javal's theories, is aimed at: (1) Overcoming suppressed vision in the squinting eye by occluding the other; (2) correcting refractive errors fully with glasses and removing any other obstacle (for example, an orbital lesion) to binocularity; (3) after this, establishing or re-establishing binocular vision by orthoptic exercises on a stereoscope; and, if necessary, (4) placing the eyes in alignment by surgery.

It has lately been confirmed[4,5] that success in recovering binocular vision depends chiefly on the age of onset of squint. If a squint arrests development of binocular vision before this is complete (that is, before three to four years), the prognosis for binocular vision is poor; if development is complete the prognosis is good.

Lyle and Foley[4] report that of those successfully regaining binocular vision the average age of onset was four years. Of their successful cases about 75 percent were accommodative squints (that is, showing a greater angle of squint for near than for distant vision), and 25 percent were nonaccommodative. All their patients with accommodative squint regained some binocular vision,

and the average age of onset was 3.3 years. Only 11 percent of patients with nonaccommodative squint regained binocular vision, and in them the average age of onset was 4.8 years. The average age in the unsuccessful cases of nonaccommodative squint was 1.8 years.

These figures emphasize that all cases of accommodative squint should be given both orthoptic and surgical treatment in full expectation of recovery of binocular vision (though it is doubtful how much orthoptic treatment contributes); whereas all cases of squint arising before three years of age may be treated by surgery alone, and much orthoptic time saved. The interval between onset and treatment averaged 1.9 years in successful cases and four years in unsuccessful cases. This reflects the need for prompt operation, though Lyle and Foley report excellent results in some cases treated late.

Naylor et al.[5] found in one group a positive correlation indicating that operation should be done within five years after onset. They could not reach a statistically significant conclusion as to whether orthoptic treatment is valuable before and after operation, since their groups treated with and without orthoptic treatment were not entirely comparable; the orthoptically treated cases had been specially selected for clinical reasons.

Lyle and Foley compared 165 patients with nonaccommodative squint who had had orthoptic treatment, with 48 who had had none, and showed little difference in results. They did not say, however, whether the conditions before treatment in the two groups were comparable.

Douglas[6] compared two groups, of 100 and 214 cases, each of which had had surgical treatment. In the first group each patient had had an average of 118 sessions of orthoptic treatment, and binocular vision developed in 35 percent. In the second series each patient had had an average of 22 sessions, and binocular vision developed in 34 percent. From these findings Douglas drew the legitimate conclusion that orthoptic treatment had had little effect.

No ophthalmologist doubts the value of an orthoptic department for help in diagnosis but some feel that orthoptic treatment may be of little value, early accurate operation after occlusion and correction of refractive error being sufficient. If this were true, much public money could be saved; or perhaps the scope of orthoptic departments might be widened to cover not only the assessment of ocular movements and binocular function, but also perimetry, scotometry, and possibly refraction.

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CORRESPONDENCE

Prevention by thyroxine of the ocular changes normally produced by IDPN

Editor,

American Journal of Ophthalmology:

The paper on "Thyroxine and IDPN lesions" by Hans Selye, which was published in The Journal (**44**:763, [Dec.] 1957), is of considerable value in many respects. Selye's experiments prove that the keratitis with degenerative changes and detachment of the retina which can be produced by IDPN is completely prevented by simultaneous treatment with Thyroxine.

In 1928 I could produce a cataract in the guinea pig's eye when barium chloride in a one-percent solution was introduced by iontophoresis at a strength of the galvanic current of three ma. during three minutes, from the positive pole only (Berliner Klin. Wchnschr., **50**:2391 [Dec.] 1928; Brit. J. Ophth., **20**:213 [Apr.] 1936). This cataract developed within 24 to 72 hours to a full "mature" cataract.

Three ways were studied to prevent the

complete mature cataract, or to clear up some of the opacities produced in the lens:

1. The combination of barium with other electrolytes and alkaloids. Only one combination prevented the cataract when barium was introduced together with a one-percent solution of ferric chloride ($FeCl_3$).

2. The second way was to treat the animal before and after the barium iontophoresis with a mixture of proteins and strychnine (XIII. Concil. Ophthal., Holland, 1:196 [Sept.] 1921).

3. The third way consisted of injecting the animal before barium iontophoresis with Thyroxine (one cc.) either intraperitoneally or subcutaneously.

In my paper on the "Scientific and practical value of ionization in ophthalmology" (Brit. J. Ophth., **20**:213 [Apr.] 1936) the barium cataract was described and the effect of Thyroxine mentioned. "It seems that Thyroxine subcutaneously injected (one cc.) before the ionization with barium has a certain effect in preventing cataract. Some sections of eyes in this experiment show an enormous dilatation of the vessels of the choroid which one never sees in any other condition."

When Selye writes that Thyroxine probably interferes with the effect of IDPN upon its chemical substrate in all tissues or that the thyroid hormone increases the rate at which the nitrile is detoxified, it can be concluded that the same assumptions may be valid for my experiments, the more so because the iontophoretically stimulated eye takes up more of an injected substance.

In this connection it is worthwhile to stress the importance of the findings of S. Ogino and his group on "Biochemical studies on cataract" (Am. J. Ophth., **43**:754 [May] 1957; **43**:936 [June] 1957; **44**:94 [July] 1957). Different cataracts were induced by various cataractogenic substances of the quinoids, which are the end-products of faulty metabolism of Tryptophane, Tyrosine, and so forth.

It would be of great basic scientific importance if the cataracts produced by barium chloride in the guinea pig's eye would become the subject of a thorough study in the light of modern methods and the aforementioned findings of Selye, Ogino, and myself. There are considerable comparative observations possible and probable.

(Signed) Gustav Erlanger, M.D.
New York

BOOK REVIEWS

ADVANCES IN OPHTHALMOLOGY: VOLUME VII. Edited by E. B. Streiff. Basel, S. Karger, 1957. 377 pages, 69 figures, 23 tables, index to volumes I-VII. Price: Swiss francs, 56.

We have learned to welcome with pleasure the appearance of these excellent reviews in their familiar blue and red bindings. Each has been a noteworthy contribution to ophthalmic literature and the present volume is no exception. Its contents include:

1. "The electro-oculography as a functional examination of the retina." This is an original and exhaustive article in French by J. François, G. Verriest, and A. De-Rouck, and describes the apparatus used, the results of experiments on normal and pathologic eyes, the relations between other methods of investigation of visual functions, the interpretation of their results, an appendix, and a bibliography.

2. "Investigation of ocular toxoplasmosis in animal experiments with special consideration of tissue reaction and morphology," in German, by W. Straub and F. Pütz. This study, based entirely on animal experiments, reveals the surprising virulence of the parasite, for example, even when dropped into the conjunctival sac and when it is injected subconjunctivally, it is recovered in the intraocular tissues. The article bears most careful study.

3. "The nature of endocrine exophthalmos," in English, by K. C. Wybar, is an excellent, up-to-date review of a complex subject.

4. "Nystagmus" is a review of the literature from 1946 to 1954 by A. Kestenbaum, who is most competent to do this job well.

5. And finally, "Biochemistry of the eye, 1946-1956," by Antoinette Pirie, the author, in collaboration with R. van Heyningen, of the well-known and recent book, *The Biochemistry of the Eye*, published in 1956 by Blackwell, Oxford. The author does a good job of a most difficult assignment for, as she points out, a comprehensive review in the advances of our knowledge of the biochemistry of the eye is coextensive with biochemistry itself. She covers the biochemistry of the cornea, the uvea and aqueous, the lens, vitreous, and retina, and visual pigments. She concludes with a plea with editors of scientific journals "to prune papers and to castigate authors for the sake of the subject and its rapid advancement."

Derrick Vail.

INTRODUCTION TO ANESTHESIA: The Principles of Safe Practice. By Robert D. Dripps, M.D., James E. Eckenhoff, M.D., and LeRoy D. Vandam, M.D. Philadelphia and London, W. B. Saunders Company. 266 pages. Price: $4.75.

Dr. Dripps and associates have done a real service for the beginner in anesthesia and for those in the medical profession interested in the principles and practice of the specialty. The book proceeds in an orderly manner to give the reader a clear conception of the approach to and evaluation of the patient, the selection of the anesthetics, and the care of the patient before, during, and after anesthesia. The chapter on the "Relationship of the surgeon and the anesthetist" is one that can be read with profit to both.

There are five main divisions dealing with certain phases of anesthetic procedures. Definitions, brief pharmacologic actions of drugs used, and an appraisal of the advantages and disadvantages of drugs and methods are most ably discussed. Special mention is accorded the chapters on "Arterial hypotension" and "Relaxant drugs."

Much of the teaching in anesthesia is passed from instructor to student by word of mouth. The authors have summed up many of these details in clear and concise form not to be found elsewhere. The subject matter is kept on the beginner's level. The more specialized aspects, as hypothermia, induced hypotension, and blocks for therapeutic uses are to be considered for more advanced study. The book is recommended reading for medical students, interns, residents, and to those who have more than a cursory interest in anesthesia.

Lucille Watt.

PRACTICAL REFRACTION. By Bernard C. Gettes, M.D. New York, Grune & Stratton, 1957. 170 pages, 58 illustrations, index. Price: $6.50.

This lucid, streamlined manual of refraction is literally made to order for the novice in ophthalmology but it still contains many pointers for the seasoned veteran. The compact, well-organized, up-to-date presentation reflects Gettes' long experience in teaching refraction at the Wills Eye Hospital and the University of Pennsylvania. The discussions on astigmatism, cycloplegic drugs, ophthalmic lenses, aphakic corrections, and aids for subnormal vision are especially noteworthy. Gettes, who directs the Visual Aid Center at Wills Eye Hospital, agrees with Fonda in a preference for high plus additions whenever feasible. For the sake of simplicity, physiologic optics, muscular anomalies, mathematical formulas, and bibliographic references have been omitted.

The entire text can be warmly endorsed except for a few minor details. The illumination of a projectochart is best controlled by an iris diaphragm, not by a rheostat as illustrated, since the rheostat changes the quality of light as well as its intensity. In discussing visual efficiency, the now official 1955 A.M.A. tables should have been utilized. The correct measurement of the interpupillary distance, certainly of practical importance, is not mentioned. Among the one-piece bifocals, Ultex K deserved inclusion. The cataract lens set and the Katral lens are no longer available, dibutolene is yet to be marketed, and the plastic binder in the shatter-

proof lens is no longer cellulose acetate but polyvinyl butyral.

This slim, moderately-priced, and very readible volume should prove a godsend to every ophthalmic resident desiring to perfect his refraction. As with other phases of ophthalmology, refraction is awfully simple if you know how, simply awful if you do not.

James E. Lebensohn.

ROENTGEN DIAGNOSIS OF UNILATERAL EXOPHTHALMOS. By M. Gazi Yasargil. Basel, New York, S. Karger, 1957. (Bibliotheca Ophthalmologica fasc. 50.) 68 pages, 26 figures. Price: Swiss francs, 10.50.

Yasargil bases his dissertation on 114 cases of unilateral exophthalmos observed in the neurosurgical department of the University Clinic of Zürich during the past 20 years. Twenty-three cases are presented with detailed histories, clinical findings, and X-ray reports. If available, the histologic findings of biopsies, surgical results, and autopsy reports are stated. The entire material is analyzed statistically. What distinguishes Yasargil's series from similar reports is the routine use of contrast dyes. In addition to percutaneous carotid angiography, the percutaneous venography of the angular vein was performed. If this method was not technically feasible, the vein was exposed. However, the injection of the vein is a much more difficult procedure than that of the artery. There were no complications among the 21 patients examined in this manner.

At first either 35- or 65-percent Nosydrast or Joduran was used as contrast media. During the past year and a half 60-percent Urografin (Schering A.G., Berlin) proved to be a more suitable material. It failed to demonstrate the ophthalmic artery in only two percent of 200 carotid angiograms. In an additional 11 percent, this artery was filled for a distance of only one or two cm. The posterior choroid was rendered visible in 74 percent of the cases seen.

The author successfully demonstrates the advantage of angiography over flat X-ray plates. This method may not always allow a specific diagnosis as to the nature of the space-taking process but such lesions can be demonstrated much more regularly than by means of flat plates. Tomography was occasionally used. The essayist warns against the use of contrast media containing iodine for orbitography in Graves' disease; he had a serious complication in one case.

The numerical distribution of cases and the types of lesions in this series are comparable to those encountered in similar reports. Yasargil cautions one to keep in mind the rare occurrence of unilateral exophthalmos as a consequence of increased intracranial pressure. Among 63 cases of meningioma of the sphenoid he saw 21 instances of unilateral exophthalmos in his series. He calls attention to reports in the literature of unilateral exophthalmos associated with sagittal meningiomas, temporal gliomas, and neurinomas of the acoustic nerve.

The material is well presented. It should be thought provoking to ophthalmologists, neurosurgeons, and roentgenologists alike.

Stefan Van Wien.

HORMONES IN BLOOD. Edited by G. E. W. Wolstenholme and E. C. P. Millar. Boston, Little, Brown and Company, 1957. 416 pages, 74 illustrations, chapter bibliographies, index. Price: $9.00.

This 11th volume of the Ciba Foundation Colloquia on Endocrinology is the largest and most technical of the series. The 35 participants include 19 from Great Britain, nine from the United States, two from Sweden, and one each from Switzerland, Belgium, Holland, Spain, and Argentina. The estimation and characterization of the hormones in the body fluids have attained a formidable state of complication. Refined and involved chemical methods are generally required and, when these are not applicable, biologic assays have been developed. The determinations of ACTH and growth hor-

mones in the blood, for example, are at present quite unsuitable for routine use in the clinical field. The hormones are affected by feed-back mechanisms that necessitate interpretation. The hypothalamus seems to elaborate a substance which regulates ACTH output. Thyroid function is related to cortisol metabolism through its influence on the metabolic rate of both the adrenal and hepatic cells. The large quantity of oxytocin in the male pituitary is one of the many puzzling facts that demand further elucidation.

In some future Colloquia the emphasis will probably be on the effect of the hormones at the cellular level rather than on the blood findings. An appended digest prepared for the general biologist would be most valuable. As it is, the contents of this Colloquia are fully intelligible only to the specialized investigator.

James E. Lebensohn.

MANAGEMENT OF COMPLICATIONS IN EYE SURGERY. Edited by R. M. Fasanella. Philadelphia and London, W. B. Saunders Company, 1957. 422 pages, illustrations and index. Price: $16.00.

Almost all textbooks of ophthalmic surgery contain a small section entitled "complications." One may wonder why a special text devoted to these complications is necessary. Dr. Fasanella answers this objection by adopting the premise that the best treatment of a surgical complication is the avoidance thereof. The scope of this book is thus enlarged to include indications for the time and type of surgical intervention in various ophthalmic disorders. For example, Dr. Berke's section on ptosis surgery is actually an excellent monograph on the subject, containing detailed and illustrated instructions for the performance of the various operations. Similarly the editor's section on lacrimal surgery compares favorably with any standard surgical text. On the other hand, sections devoted to the more common operations, such as cataract extraction and glaucoma surgery, deal only with complications, since it is presumed that the reader is familiar with standard techniques.

In addition to dealing with complications of eye surgery in a systematic fashion, the editor has included several chapters on ancillary topics that will be of special interest to the ophthalmologist. Dr. Harvey Lincoff contributes an excellent essay on psychiatric aspects of ocular surgery (although the term "exanopsic eye" grates somewhat). Dr. Leopold discusses medically responsive complications following intraocular surgery; these include intraocular hemorrhage, uveitis, infection, corneal and macular edema, and glaucoma. In spite of the title of this chapter some of the entities are not very medically responsive (nor are they surgically responsive for that matter).

Special mention should be made of the two concluding chapters. The penultimate is on the rehabilitation of the low-vision patient by Dr. Fonda. This is a conservatively presented essay that will be of great help to the ophthalmologist since it steers a middle course between the largely fatalistic approach of the professional press and the wildly enthusiastic claims of lay publications.

The final chapter is a report of a committee of the Council on Industrial Health on estimation of loss of visual efficiency. This was published in *The Archives of Industrial Health* in October, 1955, and well deserves reprinting here. Ophthalmologists who are involved in industrial medicine should use this reference constantly, and it will be a great boon to those who lecture to nonophthalmologic medical and lay groups on visual acuity and related topics.

In summary, this text is well worth careful perusal by all ophthalmic surgeons. It will be of most benefit to those who, unhappily, have personal experience with the complications described.

David Shoch.

ABSTRACT DEPARTMENT

EDITED BY DR. F. HERBERT HAESSLER

Abstracts are classified under the divisions listed below. It must be remembered that any given paper may belong to several divisions of ophthalmology, although here it is mentioned only in one. Not all of the headings will necessarily be found in any one issue of the Journal.

CLASSIFICATION

1. Anatomy, embryology, and comparative ophthalmology
2. General pathology, bacteriology, immunology
3. Vegetative physiology, biochemistry, pharmacology, toxicology
4. Physiologic optics, refraction, color vision
5. Diagnosis and therapy
6. Ocular motility
7. Conjunctiva, cornea, sclera
8. Uvea, sympathetic disease, aqueous
9. Glaucoma and ocular tension
10. Crystalline lens
11. Retina and vitreous
12. Optic nerve and chiasm
13. Neuro-ophthalmology
14. Eyeball, orbit, sinuses
15. Eyelids, lacrimal apparatus
16. Tumors
17. Injuries
18. Systemic disease and parasites
19. Congenital deformities, heredity
20. Hygiene, sociology, education, and history

1

ANATOMY, EMBRYOLOGY, AND COMPARATIVE OPHTHALMOLGY

Bembridge, B. A. **The problem of myelination in the central nervous system with special reference to the optic nerve.** Tr. Ophth. Soc. U. Kingdom **76**:311-322, 1956.

From previous experimental work the author reports that the cells of Schwann are mainly responsible for myelin production in the peripheral nervous system, but the problem for the central nervous system has not been solved. Myelin so far is a term with no accurate chemical meaning, but the important constituents are phospholipids, carbohydrate, free cholesterol and lipoprotein.

The author presents evidence that myelination proceeds toward the retinal ganglion cells, stopping at the lamina cribrosa, and that the macular fibers probably receive their sheaths before the peripheral fibers. He also showed that in the optic nerve myelination precedes function. During myelination glial cells produce lipids which form part of the myelin sheath and myelination proceeds from the chiasmal end of the nerve towards the globe. There is evidence that the axons from the macular area are among the first to receive a myelin sheath. (5 figures, 2 tables, 6 references) Beulah Cushman.

Magari, Sumiko. **The structure of the stroma of the iris and the question of an endothelial anterior surface.** Arch. f. Ophth. **159**:256-276, 1957.

The author's extensive studies of the histologic characteristics of the iris stroma are described in detail. A closely-reasoned analysis of his studies of silver impregnations of the anterior surface of the iris and reconstructions of the crypts leads him to emphasize that there are no true lymph vessels. Instead there is a network of argyrophillic fibers which may be looked upon as a system of microscopic tubules which carries dyes (which have been injected) from the anterior chamber to blood vessels. (12 figures, 34 references) F. H. Haessler.

Perez-Llorca, J., Pinero Carrion, A. and Perez Llorca, R. J. **A preliminary report on the study of the fine anatomy of the eye by means of neoprene casts.** Arch. Soc. oftal. hispano-am. **17**:553-588, June, 1957.

The technique used by the authors is a modification of the Trueta method and

consists essentially of three steps: 1. probing or intubation of the vessel or cavity to be injected, 2. irrigation, and 3. injection of neoprene. The technique and equipment for these procedures is described in detail, and 77 photomicrographs under various magnifications illustrate the results obtained on ox and human eyes. A further report will deal with the description of the vascularization of the ox eye, and the comparative vascular anatomy of the ox and human eye, particularly with reference to the suprachoroidal spaces, and the deep aqueous veins. The illustrations demonstrate the venous supply of the choroid, the vascularization of the optic nerve and large choroidal vessels, the vessels of the iris and ciliary processes, the vessels of the posterior pole, the circle of Zinn, the sclerocorneal limbus and the choriocapillaris. (77 microphotographs) Ray K. Daily.

Wolter, J. Reimer. **The structure of the nerve plexus of the sheep's cornea.** Arch. f. Ophth. **159**:291-301, 1957.

The author was unable to provide a histologic demonstration in the cornea of the sheep of a terminal network of nerves in which all types of nerve fibers coalesce and which has been said to represent the sole termination of all corneal nerves. (8 figures, 15 references)

F. H. Haessler.

2

GENERAL PATHOLOGY, BACTERIOLOGY, IMMUNOLOGY

Garzino, Alessandro. **Formation of "large bodies" in cultures of Morax-Axenfeld bacilli.** Rassegna ital. d'ottal. **26**: 193-200, May-June, 1957.

The formation of so-called "large bodies" has been observed in Moraxella lacunata (Morax-Axenfeld diplobacillus) and in many other bacteria. This fact is interesting since this is their first appearance in the life cycle of organisms which have a filterable phase. (4 figures, 19 references) Eugene M. Blake.

Kapuscinski, W. J. and Zalucki, G. **Experiments on parasympathomimetic bodies in the aqueous in hyperergic and bacterial inflammations.** Klinika Oczna **27**:227-229, 1957.

Normal rabbit aqueous had no effect on the frequency and amplitude of the beat of the frog's heart. Aqueous of rabbit with bacterial iritis also had no effect but aqueous of allergic iritis definitely slowed heart rhythm and decreased the amplitude of contractions. Additional experiments were made on anesthetised cats. After injection of allergic aqueous their blood pressure fell 20 to 35 mm. Hg. Similar reactions were obtained after injections of histamine and acetylcholine. (1 figure, 3 references) Sylvan Brandon.

Mizukawa, T., Kizu, S., Kido, R. and Konishi, K. **Ocular allergy by lens protein.** Acta Soc. Ophth. Japan **61**:1452-1456, Sept., 1957.

A small amount of Schwarzman's filtrate was injected into rabbits intravenously. Twenty-four hours later, 0.1 ml. of freshly prepared one-percent solution of bovine lens protein was introduced into the anterior chamber of one eye. A precipitation reaction became positive in the aqueous of the associate eye and also in the blood stream in the course of ten days. Then an injection of the antigen into the associate eye resulted in the onset of a characteristic allergic reaction. The authors believe that absorption of the antigen was accelerated by an injection of Schwarzman toxin and, therefore, a systemic sensitization was brought about even by the injection of such a small amount of the antigen into the aqueous. (3 figures, 4 tables, 24 references)

Yukihiko Mitsui.

Mueller, Fritz. **Interpretation of bacteriologic examination and determination of resistances in ocular diseases.** Klin. Monatsbl. f. Augenh. **131**:352-363, 1957.

1,812 bacteriologic examinations of conjunctiva, cornea, lid, lacrimal pathways, vitreous, aqueous and blood were done in infectious eye diseases. Staphylococcus albus was most frequently found, then S. aureus, streptococcus and Gram-negative rods. It was found that 45 percent of the microorganisms were sensitive to penicillin and 71 percent to chloramphenicol. (4 tables, 15 references)

Frederick C. Blodi.

Ogielski, L., Kapuscinski, W. J. and Ogielska, E. **Biochemical color reaction in experimental hyperergic and bacterial inflammations.** Klinika Oczna **27**:215-219, 1957.

Two series of experiments were arranged. In the first series allergic iritis was produced in rabbits. In the second staphylococcus aureus was introduced into the anterior chamber. In the first series color tests of Kolobolocki were negative, in the second group they were positive. In human iritis the color test is usually positive, suggesting the presence of bacterial toxins in the aqueous. (24 references) Sylvan Brandon.

Wolter, J. Reimer. **Beadchain-like degeneration of nerve fibers in the human optic nerve.** Arch. f. Ophth. **159**:385-390, 1957.

The author describes a new histopathologic finding and its significance. It is adequately characterized in the title. (6 figures, 6 references) F. H. Haessler.

3

VEGETATIVE PHYSIOLOGY, BIOCHEMISTRY, PHARMACOLOGY, TOXICOLOGY

van Alphen, G. W. H. M. **Acetylcholine synthesis in corneal epithelium.** A.M.A. Arch. Ophth. **58**:449-451, Sept., 1957.

von Brücke has reported a remarkably high concentration of acetylcholine in the corneal epithelium and almost none in the stroma. The experiments related in this paper document a cholinacetylase which will synthesize 1,000 y of acetylcholine per gram per hour. The role of the acetylcholine in corneal health is considered. (1 table, 17 references) G. S. Tyner.

Bleichert, A. **The light reaction of the pupil as a process of regulation.** Arch. f. Ophth. **159**:396-410, 1957.

The author analyses the reaction of the pupil to light as a widely integrated biological regulatory process rather than a simple reflex. This is in no sense a question of terminology but fundamentally an extension of our understanding of the sequence of progression in a biologic function. In the place of an open causal chain of cause and effect of the old reflex sequence he examines the closed causal chains in cycles of function. He bases his analysis on statistical study of patterns and on dynamic observations. (7 figures, 23 references) F. H. Haessler.

Csanda, E. and Bohár, A. **Experimental contributions to the parallelism of vessel permeability in brain and eye.** Szemeszet **2**:49-63, 1957.

The authors discuss the modern theory of capillary permeability and point out the significance and value of vital staining procedures. The analogy between the capillary permeability of the retina and that of the central nervous system was stressed in 1913 by Rados, in 1947 by Palm. In contradistinction to this, Sautter observed in 1954, likewise by vital staining, the different behavior of the retina. Broman stressed the sources of error resulting from vital staining. Starting from the theoretical and practical importance of the problem, the authors carried out examinations with acid and basic vital dyes (trypan blue, Ewans blue, methyl

green, Geigy blue, anilin red and with triphenyl-tetrazolium chloride which is considerably more sensitive than the others) in 25 cats, 21 rabbits, and 14 rats. First the examinations were done with ophthalmoscopic control, then blood and dye were washed out of the vessels of the head by perfusion, eye and brain were fixed with the same method and examined grossly and microscopically. Acid vital dyes did not stain the retina like the gray matter, and the optic nerve like the white matter. Basic dyes escaped through the vessel wall immediately. Iris and ciliary body displayed positive staining behavior like the choroid plexus, the dura mater behaved like the sclera. The choroid behaved like the pia mater but stained, unlike the pia, after the administration of a greater amount of dye. Triphenyltetrazolium chloride acted as a redox indicator and converted, having come in contact with the tissues, to the red reduction product crystalline formazane. Despite their high redox potential, retina and brain cortex remained unstained because of a barrier functioning between tissues and capillaries. This barrier is highly resistant: several hours after the killing of the animal it is still impermeable to acid vital dyes and preserves its integrity even if lethal doses of histamine, acetylcholine, and hydergin act on it.

Gyula Lugossy.

Desvignes, P. and Seigneur. **Clinical study of a new surface anesthetic for ophthalmology: cornecaïne.** Arch. d'opht. **17**:473-475, 1957.

The authors report a clinical study of a new surface-acting anesthetic called "cornecaïne" (p-propyl-amino-benzoic ester of dimethylaminopropandiol) prepared by Dr. L. Stein. It is used as a chlorhydrate, and aqueous solutions are compatible with other drugs used in ophthalmology. It is toxic by subcutaneous injection but well tolerated topically and reported as being seven times more active than cocaine. In their study the authors found a 1-percent solution satisfactory for tonometry and for removal of foreign bodies, and a 3-percent solution preferable for preoperative anesthesia in cataract extraction. The drug was only slightly irritating, had no effect on the pupil, on accommodation, or on ocular tension, and did not desquamate corneal epithelium or produce allergic reactions. (7 references)

P. Thygeson.

Gittler, R., Pillat, B., Pommer, H. and Stumpf, C. **The dependence of the entrance of fluoresceine into the aqueous upon angioactive substances.** Arch. f. Ophth. **159**:359-368, 1957.

In experiments on rabbits it was found that the vasoconstriction of the iris vessels depressed the entrance of fluoresceine into the aqueous and vasodilators stimulated it. The transference of fluoresceine may be ascribed directly to the capillary pressure. (2 figures, 28 references)

F. H. Haessler.

Kapuscinski, W. J., Szczudlowski, K. and Popadiuk, L. **Experimental jet pulse on the mesentery artery of a dog.** Klinika Oczna. **27**:263-268, 1957.

The authors explain the mechanism of the jet pulse present in the mesentery of a dog. A model explains why the jet pulse disappears in cases with choked disc. (3 figures, 8 references) Sylvan Brandon.

Katsumori, Y. **Changes in the distribution of lens protein during the development of cataract.** Acta Soc. Ophth. Japan **61**:1457-1468, Sept.. 1957.

The change in the lens protein during the development of cataract is studied in relation to naphthalene cataract in rabbits. During the development of cataract, there occurs a gradual reduction in soluble protein of the lens crystallines, with an increase in residual nitrogen and in-

soluble proteins. (13 figures, 5 tables, 24 references) Yukihiko Mitsui.

Magdalena Castineira, Jaime. **Pressure in the aqueous veins.** Arch. Soc. oftal. hispano-am. **17**:462-467, May, 1957.

The author divides the aqueous veins into three types: 1. veins filled with aqueous only, 2. veins filled with a mixture of venous blood and aqueous, and 3. laminated veins in which two distinct currents are visible. This study deals with the vessels containing a mixture of blood and aqueous of 150 eyes. The vessels selected for study were large with but little anastomosis. A small cylindrical pressure chamber 6 mm. in diameter was applied over the vessel and the pressure measured by means of a water manometer connected to the pressure chamber by a rubber tube. This was done under slitlamp observation. In 40 normal eyes the average pressure was 10.15 mm. of mercury. In 30 glaucomatous eyes the tension of the aqueous veins was generally raised, but not proportionately to the elevation in ocular tension. In 24-hour curves there is evident a parallelism between the pressure in the aqueous veins and the ocular tension, the pressure in the veins falling in advance of the fall in the intraocular pressure. The author believes that clinically the diagnostic tests of the aqueous veins do not carry much significance. The aqueous veins are but a portion of the drainage system of the globe and they do not function under the same conditions as the deeper drainage channels. The intrabulbar veins must maintain pressure greater, equal to, or but slightly lower than the ocular tension, or they would collapse. On reaching the sclera the pressure within the veins falls, because the tough sclera protects them and outside the sclera it rapidly equals the pressure of the veins on the face. The anastomosis with the conjunctival veins produces marked and unequal variations in the pressure of the aqueous veins, depending on the vessel which is explored. The author has seen some of the aqueous veins of the same eye follow the oscillations in the intraocular pressure, while other veins did not. He attaches greater importance to the deeper drainage channels. In the early stages of glaucoma the oscillations in the ocular tension are due to functional changes in the vessels of the drainage channels. In advanced glaucoma the sclerosis of the ocular blood vessels raises the base of the ocular tension, and the variations in the pressure of the aqueous veins is greater the higher the ocular tension, and the greater the vascular lability of the patient. (3 figures, 2 graphs) Ray K. Daily.

Ogielska, Eugenia. **Dynamic cytogram in experimental iritis.** Klinika Oczna **27**: 221-226, 1957.

Experiments were conducted on two groups of rabbits: one with bacterial iritis and the other one with allergic iritis (horse serum). Aqueous was repeatedly withdrawn until it became normal. The first puncture produced erythrocytes, leukocytes, lymphocytes and a few monocytes and histiocytes. Gradual decrease in inflammation was paralleled by disappearance of blood cells and proportionate increase in cells of the reticulo-endothelial system. There was no difference in the cytogram of the aqueous of bacterial and allergic iritis. The dynamic cytogram in human iritis presents a similar picture and cannot be used in differentiation between bacterial and allergic inflammation. However, it makes it possible to evaluate the processes of defense and may be used for prognosis. (2 tables) Sylvan Brandon.

Pfeifer, H. **The action of helenien on normal and reduced dark adaptation.** Arch. f. Ophth. **159**:311-322, 1957.

Pfeifer studied the effect of the carotinoid helenien to determine whether this

substance can bring about dark adaptation greater than normal. He divided 22 normal subjects into three groups each of which was given a different dose of helenien (5, 10 and 100 mg.) daily for two weeks. It was found impossible to extend dark adaptation beyond normal. Similar experiments were done with 13 subjects who had reduced dark adaptation and myopia, retinitis pigmentosa or choroiditis. In two of the subjects with myopia there was a slight improvement after the course of ingestion of helenien. (5 figures, 3 tables, 14 references)

F. H. Haessler.

Sergienko, S. **Biochemical reactions in the protein fractions of the blood on phlyctenular diseases of the eye.** Vestnik oftal. **3**:6-10, May-June, 1957.

The author studied the therapeutic value of Pask (Pas) in 112 patients, aged from four to 28 years, with various phlyctenular diseases; in 30 of these, the protein fractions of the blood were examined before and after treatment.

The condition of the protein fractions of the blood is a measure of the allergy. The amount of protein is the lowest normal. The albumen-globulin coefficient before treatment is markedly decreased (0.87). There is a certain parallelism between the Mantoux reaction and the degree of the decrease of the albumen-globulin coefficient: the more marked the Mantoux reaction, the lower the coefficient. The albumen-globulin coefficient is increased under the treatment with Pask: the albumen fraction is increased and the globulin fraction is decreased. The average is 1.46. The improvement of the albumen-globulin fraction under treatment with Pask indicates that Pask decreases the allergic state. The degree of the increase of the albumen-globulin coefficient indicates the stability of the therapeutic effect. (1 drawing, 3 tables)

Olga Sitchevska.

Szeghy, G. **The pathophysiology of the cornea. I.** Szemeszet **1**:1-6, 1957.

In narcosis individual vascular areas of the conjunctiva of rabbits can be well examined with the epicondensor microscope. The effect of locally administered drugs can be well observed. If the cornea is intact, acetylcholine dilates the conjunctival vessels. The response of vessels to adrenalin is particularly weak at the limbus. If the cornea is damaged the vessels in an area of the limbus corresponding to the sector of damage display an increased response to adrenalin despite the vasodilation. This area becomes larger with time. In this case, the effective dose of adrenalin is lower than in the case of intact cornea. The adrenalin cannot be influenced by antihistamine given locally or parenterally. Glanduitrin and barium chloride fail to produce the phenomenon.

The experimental data suggest that a substance enhancing the effect of adrenalin is released at the place of damage and spreads circularly. Of this substance a certain concentration is needed to bring about vascularization of the cornea. The substance bringing about vascularization is not histamin.

Gyula Lugossy.

Szeghy, G. **The pathophysiology of the cornea. II.** Szemeszet **2**:64-70, 1957.

The isolated cornea of cattle put into various solutions absorbs the greatest amount of fluid in the first hour. Its weight increase per hour decreases in the following hours gradually but slowly. The quantity of fluid absorbed depends on the area of surface of the organ in contact with the fluid. In hypertonic solutions the initial absorption decreases and the process of absorption becomes uniform.

Protamine sulfate and lysozyme acting on the mucopolysaccharides exert, in low concentration, no influence on the initial fluid absorption, but reduce total absorption. After protamine sulfate and lysozyme have combined with the mucopolysac-

charides, corneal discs absorb little or no distilled water. The mucopolysaccharide content of the solution has no influence on fluid absorption. Fluid absorption results in blurring of the cornea. The grade of blurring depends on the concentration of the fluid and the concentration of the substances acting on the mucopolysaccharides. Swelling increases in proportion to the amount of the fluid absorbed. During fluid absorption by the cornea a substance becomes dissolved and precipitates with protamine sulfate and lysozyme. This substance is the protein-bound water-soluble form of mucopolysaccharide. The corneal disc which has lost its transparency under the effect of protamine sulfate and lysozyme becomes, after drying, transparent to the same extent as one placed in distilled water or sodium chloride.

Gyula Lugossy.

Wozniakowa, Irena. **Influence of removal of possible primary focus on permeability of blood-aqueous barrier.** Klinika Oczna **27**:255-258, 1957.

The author investigated the permeability of the blood-aqueous barrier in 20 patients with iritis. Amsler's method of fluorescein determination in the aqueous was used. In all of these patients dead teeth were found and extracted and in all permeability of the blood-aqueous barrier increased despite the fact that not all of the extracted teeth looked like possible foci of infection. The author discusses the reaction to tooth extraction. (1 figure, 3 references) Sylvan Brandon.

4

PHYSIOLOGIC OPTICS, REFRACTION, COLOR VISION

Allen, Frank. **The measurements of visual action-time of McDougall.** Acta ophth. **35**:20-25, 1957.

McDougall's original investigations on visual action time were reported numerically but not graphically. In this study the author plots McDougall's data. The linear character of the graphs indicates that the action time varies inversely with the logarithm of the intensity of stimulation, within the same limits, and with different numerical values of the proportionality constant for different ranges of intensity. The author designates this principle as the McDougall's law of action-time. (3 graphs, 4 tables, 6 references)

Ray K. Daily.

Blackwell, H. R. **Quantitative relationships of illumination and vision.** Arch. Indust. Health **16**:108-121, Aug., 1957.

This presentation is a simple enumeration of various experiments performed to demonstrate certain basic principles. The conclusions may be listed as follows. A marked increase in luminance will increase visual speed and accuracy. When the visual task is very small, increased luminance is not as dramatically helpful. A great deal more light is required for a rectangular object than for a circular one, and it takes more light to see a cross than a circle of equal area. Extrafoveal perception requires a great deal of luminance for equal performance. Glare and nonuniformity of light decrease visual efficiency, but the more luminance is added, the less important these problems become. The amplitude of accommodation is decreased by reducing the light level. The accommodative portion of vergence is critically affected by illumination. Highly saturated colors at either end of the spectrum cause some ocular blurring, with accompanying decrease in visual performance and comfort. Harry Horwich.

Bonnet, P. and Rougier, J. **The role of the sympathetic in accommodation.** Arch. d'opht. **17**:221-249, 1957.

The authors have reviewed the subject of the role of the sympathetic in accommodation, beginning with the observa-

tions of Brucke in 1846. They discuss in detail the Helmholtz theory of accommodation and evaluate the evidence, experimental and clinical, bearing on it. They stress that studies of the past few years, notably those of Cogan and of Olmstead and collaborators, have served to clarify the role of the sympathetic. Among these may be mentioned the observation that paralysis of the cervical sympathetic leads to disturbance in adaptation for distant vision, and that excitation of the cervical sympathetic interferes with accommodation for near vision. The authors conclude that the sympathetic plays a definite role in accommodation and that it is concerned principally with adaptation for distant vision. (87 references) P. Thygeson.

Bornschein, H. and Goodman, G. **Studies of the a-wave in the human electroretinogram.** A.M.A. Arch. Ophth. **58**: 431-437, Sept., 1957.

The electroretinogram in response to high-intensity stimuli represents a sequence of waves beginning with a negative deflection, the a-wave. The present study deals with the a-wave of normal, congenitally night blind, and totally color blind subjects in response to white stimuli of different intensities. (7 figures, 16 references) G. S. Tyner.

François, J. and Verriest, G. **State of our knowledge of color vision in the animal kingdom.** Ann. d'ocul. **190**:633-683, Sept., 1957.

Although color vision is thought to be a subjective response of man to certain wave-lengths of light, the authors show that the response to these wave lengths can be studied in lower animals. They review four methods of study: histologic examination of the retina, reactions to light stimulus (pupillary reflexes, opticokinetic responses, conditioned reflexes), electrophysiologic methods and biochemical study of visual pigments. They then present data for selected species in each of the major phyla. They thus demonstrate that color vision is almost always present where there is a differentiated visual structure. The assumptions which lead to this conclusion are: a visual cell whose spectral sensitivity corresponds to rhodopsin is a rod while one whose spectral sensitivity shows a shift to the longer wave lengths is considered a cone; all phyla show at least a potential retinal duality although there may be secondary loss of either the rods or cones; there may be adaptations by residual rods for cone function or vice versa. From these studies the authors conclude that human color-deficiencies are due to accidental mutations rather than to "atavism." (3 figures, 197 references) David Shoch.

Goar, Everett L. **Contact lenses in monocular aphakia.** A.M.A. Arch. Ophth. **58**:417-420, Sept., 1957.

Goar reports on the use of the contact lens in monocular aphakia in 63 patients. Of 13 patients who have had the second eye operated upon, ten wear contact lenses binocularly. The author pleads for more general use of the method. (8 references) G. S. Tyner.

Helms, A., Krüger, R. and Strässner, H. **Changes in the sensitivity of the dark-adapted human eye during monocular adaptation.** Arch. f. Ophth. **159**:369-370, 1957.

Three experienced observers made 11 determinations in each of two series of measurements and the results show great agreement. After dark adaptation of both eyes the right was exposed to 300 flashes of light of short duration ($t = 0.1$ sec. $\lambda = 500$ mμ) in groups of 100 each. Then the still dark-adapted left eye was made light-adapted by exposure to the artificially illuminated room. In the second series measurements were made with an observing dark-adapted right eye and a left

eye which had been made light-adapted as before and groups of 100 flashes of light were given at intervals of 10 minutes. (1 figure, 2 references)

F. H. Haessler.

Kato, K. and Tabata, S. **The hue discrimination of normal and color defective subjects.** Acta Soc. Ophth. Japan **61**:1647-1655, Sept., 1957.

This is a study on the hue discrimination of normal and anomalous individuals. A modified type 2 anomaloscope was used. Normal persons can differentiate two hues having the wave difference of less than 3 mμ except for the range of wave-length over 630 mμ. The normal discrimination curve has three minima in most cases and they are found at the wave-lengths 440-450, 480-500, and 580-600 mμ. The discrimination curve of protanopsia and deuteranopsia is a parabola having one minimum at wave-length 480-490 mμ. At this point protanopes can differentiate the wave-length of 4 mμ and deuteranopes of 1.4 mμ. The curves of protanomalous and normal persons are much the same. The curves of the deuteranomalous subject has no definite form, however. In some cases the curve is nearly normal and in some others it resembles that of deuteranopia. (6 figures, 3 tables, 6 references)

Yukihiko Mitsui.

Mahneke, Axel. **Comparison between the continuous and discontinuous method in flicker fusion thresholds.** Acta Opht. **35**:53-61, 1957.

The author uses the symbol t_{d-c} for the flicker fusion threshold determined by using low frequency to start, and increasing it until the observer reports a change from a flickering to a fused light. For the threshold obtained by beginning with a frequency above the fusion limit and lowering it until the observer recognizes the change from a fused to a flickering light he uses the symbol t_{c-d}. These are the procedures used for the determination of the threshold by the continuous method. In the discontinuous method the observer is confronted with a constant frequency at one time; he reports whether he perceives a flickering or fused light. The influence of difficulties of fixation, local adaptation and varying contrasts on the results are discussed.

The data on the comparison of the two methods of investigation show that the threshold values determined by the discontinuous method are grouped above or around the continuous flicker fusion threshold t_{c-d}. The continuous t_{d-c} threshold was lower. The experiments have thus confirmed the difference between the two flicker thresholds determined by the continuous method. The cause of the difference is difficult to elucidate; absence of firm fixation of the light source, local adaptation and summation of after-images are factors to be considered. The method of accelerating the frequency appears to be most important in the relation of the two continuous methods. The author concludes that the continuous t_{c-d} threshold reflects better the property our eyes have of following the intermittence in a discontinuous light stimulus with a varying frequency. The continuous t_{d-c} flicker threshold also reflects this property, but is affected by other components. The practical implications of this investigation are that the method of choice is a discontinuous threshold determination with an exposure period of five to six seconds, or the continuous fusion flicker threshold determination (t_{d-c}). (1 figure, 1 table, 5 references)

Ray K. Daily.

Martin, L. **A preliminary biometric study on the recovery of the luminosity curve as registered on the adaptometer of Goldman-Weekers.** Bull. Soc. belge d'opht. **115**:205-210, 1957.

The adaptation curve as determined on the Goldmann-Weekers adaptometer represents the time as abscissa. The curve consists of two components of unequal slope and represents two segments formed by a rather large number of points (log 1+). The reduction of these data to a smaller number of parameters was considered to be a biometric problem. The transformation of the graphs and the basic causes for those changes are described. (2 figures, 6 references)

Alice R. Deutsch.

Momose, A. **Quantum biophysics of vision. II.** Acta Soc. Ophth. Japan **61**:1593-1620, Sept., 1957.

To determine the threshold number of light quanta which must act upon the visual receptors to elicit a visual sensation, experiments were conducted on the completely dark-adapted retina of the author's eye, using the method originally designed by Hecht and his co-workers. The threshold number was shown to be 7. When the method designed by Van der Velden was employed the number was 2. Momose believes, however, that the latter method is not reliable. (6 figures, 1 table, 25 references) Yukihiko Mitsui.

Schenk, H. and Pfeifer, H. **Dark adaptation in aphakia.** Arch. f. Ophth. **159**:285-290, 1957.

The authors determined the dark adaptation with a Goldmann-Weekers adaptometer in three aphakic patients and in 32 normal controls. A slight hemeralopia was demonstrable in all aphakic subjects. The decreased ability of the aphakic eye to become adapted is ascribed to excessive light adaptation which develops after extraction of the lens because rays of wave length of 3000 to 3300 Å, which are filtered out by the normal lens, reach the retina in its absence. (3 figures, 11 references)

F. H. Haessler.

Shibata, H. and Kanki, K. **Change in refraction in high myopia by lens extraction.** Acta Soc. Ophth. Japan **61**:1683-1693, Sept., 1957.

The results in 170 eyes are summarized. The reduction in the refraction by surgery was in the range of 17 and 37 diopters with the average of 22.5 diopters. In 98 of the 170 eyes the postoperative refraction was in the range of +1.0 and −1.0 diopters. The refraction before surgery was in the range between −16 and −30 diopters. A higher reduction in the refraction was obtained in cases with higher degrees of myopia and the authors believe that "lens myopia" plays a role even in the high myopia. (3 figures, 11 tables, 11 references) Yukihiko Mitsui.

Spaeth, E. B. **Discussion of the estimation of loss of visual efficiency.** Arch. Indust. Health **16**:104-107, Aug., 1957.

The general principles of the Joint Committee report on revision of estimation of loss of visual efficiency are briefly presented. The report itself is considered, by the committee, impossible of abstraction.

The first subdivision consists of four sections, a. essential factors in determining visual efficiency, b. determination of central acuity for far and near, c. estimation of efficiency of an impaired field, and d. loss of efficiency due to disturbance of motility.

The second subdivision consists of calculations for visual efficiency, taking these factors and corrected vision into account. Certain important changes are: 1. that best corrected acuity be used, 2. that the relative inequities between very poor and slightly poor acuities be made more realistic, 3. that the importance of diminished near acuity be given full weight, and 4. that a mathematical formula for calculating the degree of disability caused by loss of binocular vision be considered.

Harry Horwich.

Szucs, S. and Coppez, L. **A comparative study of the dark adaptation of normal and diabetic eyes (a preliminary report).** Bull. Soc. belge d'opht. **115**:190-205, 1957.

The Goldmann-Weekers classical procedures for the retina were used. After a preliminary period of adaptation of seven or eight minutes in half darkness and two minutes in total darkness the patients were exposed to 2,000 to 3,000 Lux for five minutes. It was thought essential to have the preadaptation time and period of exposure to light identical during each examination. Anomalies of refraction were corrected to 9/10 or 10/10 visual acuity. The adaptation curves were plotted in complete darkness and registered on automatic drums. The normal coefficient of adaptation was determined at about 40 with minimal variations dependent on age. It reached 3.00 to 2.8 in diabetics (three patients less than 30 years of age, 13 patients between 42 and 63 years of age). A considerable reduction of adaptation in diabetics was therefore recognized. It was, however, acknowledged that neither vascular complications and retinopathies nor the duration of the metabolic disease were of special significance and could not be made responsible for the slowness in adaptation. The role of concurrent vitamin A insufficiency is explained. (5 figures, 2 tables) Alice R. Deutsch.

Unger, Hanns-Hellmuth. **Changes of the ciliary band during accommodation.** Klin. Monatsbl. f. Augenh. **131**:385-395, 1957.

Examined were 250 eyes. The band was measured by goniometry (Four-mirror-gonioscope and measuring ocular). Cycloplegics (atropine, scopolamine) enlarge the ciliary band while miotics usually narrow it. One normal, enucleated globe was opened meridionally. One half was put into 2 percent pilocarpine and the other half into 1 percent atropine for five minutes. Rapid fixation followed. The ciliary part of the chamber angle was wide after atropine and narrow after pilocarpine. Generally speaking the ciliary band will be wide in myopia and in accommodation paralysis. It will be narrow in hyperopia, presbyopia and in spasm of accommodation. (6 figures, 1 table, 30 references)

Frederick C. Blodi.

5

DIAGNOSIS AND THERAPY

Abramowicz, Ignacy. **Eye surgery in the deaf and dumb.** Klinika Oczna **27**:299-300, 1957.

The author suggests that a certain number of touch signals should be arranged before surgery is undertaken.

Sylvan Brandon.

Agarwal, L. P., Gupta, R. B. L. and Malik, S. R. K. **Chlorpromazine in ocular surgery.** Brit J. Ophth. **41**:565-569, Sept., 1957.

In this study 105 intraocular operations were performed under the combination of nembutal and 50 mg. chlorpromazine given intramuscularly; in addition routine local anesthesia was used. The patients were more relaxed and freer from mental tension and apprehension though probably not as much as with curare preparations. The drug was also given by mouth for several days to lessen postoperative tension. (4 tables, 7 references)

Morris Kaplan.

Aguilar Bartolome, Jose M. **Diagnosis and treatment of viral diseases of the anterior ocular segment.** Arch. Soc. oftal. hispano-am. **17**:779-920, Aug., 1957.

This exhaustive monograph on the subject is divided into five chapters of which the first deals with a description of viruses in general as to size, shape, structure, metabolism, culture characteristics, diagnostic methods, allergy, and classification. The last four chapters are devoted to the viruses causing ocular diseases and to a

description of the ocular lesions, and their diagnosis and treatment. (39 figures, 11 tables, 215 references) Ray K. Daily.

Asher, H. **The fixator.** Brit. J. Ophth. **41**:622-625, Oct., 1957.

An apparatus devised to test binocular fixation as well as the visual efficiency of each eye at near is described. (3 figures) Lawrence L. Garner.

Baum, Gilbert. **Evaluation of the techniques used in the radiation of the eye with ultrasonic energy.** Am. J. Phys. Med. **36**:212-220, Aug., 1957.

A method for the application of therapy with ultrasound radiation is described and the author points out that this method of therapy is still in the realm of experiment. (5 figures, 4 tables, 36 references) Irwin E. Gaynon.

Böke, W. and Conrads, H. **The histology of the cornea in acute keratoconus.** Arch. f. Ophth. **159**:277-284, 1957.

The histologic changes in the cornea with acute keratoconus throw no light on the cause of acute keratoconus. In the apical region of the conus there is a condensation of the intercellular substance of the corneal stroma, a polar arrangement of the parenchymal cells, a circumscribed proliferation of epithelial cells over Descemet's membrane and a transition to scar tissue. The corneal nerves are morphologically intact and the corneal epithelium shows degenerative changes such as seen in other corneal lesions. (9 figures, 19 references) F. H. Haessler.

Bosso, Giancarlo. **Electrophoresis of the aqueous in inflammatory condition of the anterior segment of the eye.** Rassegna ital. d'ottal. **26**:127-138, March-April, 1957.

The aqueous humor was studied in nine patients. There was a considerable increase in the protein content of the aqueous in patients with corneal lesions associated with iridocyclitis. Study showed that the protein content was about normal as compared to that of the blood. Lipoproteins, however, were evident only in cases of secondary corneal involvement, but were absent in iridocyclitis. The author suggests that the protein arises in tissues contiguous to the aqueous in inflammatory processes of the anterior portion of the eyeball. (5 tables, 16 references) Eugene M. Blake.

Breinin, G. M. **New aspects of ophthalmoneurologic diagnosis.** A.M.A. Arch. Ophth. **58**:375-388, Sept., 1957.

Breinin reports his extensive experiences in using the technique of electromyography on various extraocular muscle disorders, especially of the neurogenic types. (29 figures and 11 references) G. S. Tyner.

Colombi, Carlo. **The effect of ophthalmic ointments in the anterior chamber.** Rassegna ital. d'ottal. **26**:91-100, March-April, 1957.

The common greasy ophthalmic ointments which sometimes accidentally enter the anterior chamber may produce sensible damage, even though in small amounts they may cause changes less than actual uveitis. The ointment may gradually disappear spontaneously in time. The composition of the excipient and the medicament cause variable changes. Frequently, the small amount of ointment may lie in the angle and be overlooked, especially if there is a gerontoxon. (12 figures, 19 references) Eugene M. Blake.

Comberg, W. **Improvements of the simplified light sense test.** Klin. Monatsbl. f. Augenh. **131**:289-292, 1957.

In this test, originally described in 1940, light perception is measured through the

closed lids. It can be made quantitative by increasing the distance of the light from one eye until the subjective light intensity equals that of the other eye. The light source can be varied by a diaphragm. A contact glass of opaque material can be inserted if lid closure is impossible or if the lids are pathologically changed. (4 figures, 3 references) Frederick C. Blodi.

Decker, K. and Schlegel, H. J. **Normal and normally variant roentgenologic patterns of the ophthalmic artery.** Arch. f. Ophth. **159**:302-310, 1957.

The roentgenograms of the ophthalmic artery of greatest diagnostic reliability are made by automatic serial roentgenography (up to six exposures per second). Both the proximal and distal segments of the artery are subject to much anatomic variation and in the roentgenogram further difficulty is introduced in that a complex three-dimensional structure is rendered two-dimensionally. The authors describe variant patterns and discuss their significance. (12 figures, 9 references) F. H. Haessler.

Dejean, Ch. and Prat-Flottes. **The usefulness of systematic examination of the eye in the tuberculous infant.** Arch. d'opht. **17**:445-454, 1957.

The authors report fundus findings in 12 tuberculous infants with past or present meningitis. They conclude that the classical acute or subacute form of tuberculous meningitis is not the only one seen in infants; that there exist also chronic forms localized to the basal areas which can evolve insidiously. These chronic forms can extend and explode suddenly into severe and unexpected activity. Examination of the fundus, and particularly of the optic nerve with its close meningeal association, can often uncover these chronic forms at a time when antituberculous therapy can be employed effectively. (10 figures) P. Thygeson.

Dessoff, Joseph. **Paracentral homonymous hemianopic scotoma.** A.M.A. Arch. Ophth. **58**:452-454, Sept., 1957.

Paracentral homonymous hemianopic scotoma is a rare field defect and the exact location of the lesion is uncertain. However, sudden inability to read in the presence of normal fundi, normal visual acuity, and normal peripheral fields should make one suspect this syndrome. (2 figures, 4 references) G. S. Tyner.

Drozdowska, S. and Nowicka, S. **Statistics of fever therapy with typhoid vaccine.** Klinika Oczna **27**:233-238, 1957.

A statistical analysis of treatment with typhoid vaccine of 1,388 eye patients is presented. It was most successful in cases of uveitis, particularly iritis and cyclitis. It helped in scleritis and episcleritis and in secondary inflammations in injuries and after surgery. Optic neuritis and sympathetic ophthalmia did not respond so well. Diseases of the cornea and the retina were not affected by this treatment. Uveitis, where typhoid vaccine was contraindicated, responded to the usual treatment considerably more slowly and the treatment was not always successful. (2 figures) Sylvan Brandon.

Farnsworth, Dean. **Testing for color deficiency in industry.** Arch. Indust. Health **16**:100-103, Aug., 1957.

A classification for color deficiency is suggested, which lists protan, deutan, and tritan across mild, moderate and severe. Mild color defectives have little disability in most types of work, and should not be arbitrarily excluded. Workers with a moderate defect can usually do well under optimal and controlled conditions and those with severe defects should never be placed in a situation where color discrimination is important. The American Optical Co. or Ishihara plates under the Macbeth lamp are recommended for screening and, when greater refinement of testing is necessary,

the Farnsworth lantern and the dichotomous test. Harry Horwich.

Fernandez, R. H. P. and Watkins, J. T. **Portable eye irrigation unit.** Brit. J. Ophth. **41**:626-628, Oct., 1957.

A portable wooden case containing a glass container of normal saline solution is described. This was devised originally by rescue teams in mines for emergency irrigation of eyes irritated by acid fumes. However, it provides a handy means of sterile and quick irrigation in any treatment center. (2 figures)

Lawrence L. Garner.

Foote, F. M. **Components of a complete vision program.** Arch. Indust. Health **16**: 91-92, Aug., 1957.

The reasons for having a complete industrial vision program are listed. They include saving vision, lowering compensation and insurance costs, apt placement according to visual skills, screening for eye disease, decreased absenteeism, less waste, and increased production.

Six basic points in such a program are stressed: 1. testing of the five fundamental visual skills which are vision at distance and near, muscle balance, depth perception, and color discrimination, and screening for disease; 2. job analysis for visual factors; 3. provision of eye safety equipment; 4. proper and convenient provision of eye emergency care; 5. proper use of illumination and color; 6. group and individual education in eye health and eye safety. Harry Horwich.

Goldin, R. R. and Silver, M. L. **Ophthalmic artery aneurysms.** Radiology **68**: 727-730, May, 1957.

The authors describe a 50-year-old female patient who was found to have an aneurysm of the ophthalmic artery and a thrombus within it. The patient's disease was characterized by a progressive diminution of vision for three months which ended in light perception. Fundus examination revealed optic atrophy.

In retrospect the authors believe that a suggestion of the diagnosis was made by views of the optic foramena which, on the affected side showed erosion of the temporal aspect of the optic foramen. This is the portion of the foramen occupied by the ophthalmic artery. (3 figures, 2 references) Alan S. Freemond.

Goldsmith, A. J. B., Lederman, M. and Dudgeon, J. A. **Symposium. Herpetic infections of the outer eye.** Tr. Ophth. Soc. U. Kingdom **76**:187-225, 1956.

Goldsmith, A. J. B. **Herpes simplex-zoster.** pp. 187-192.

Corneal manifestations of herpes simplex such as dendritic ulcers often accompany a cold or infection of the upper respiratory tract or mild corneal trauma. The only way to relieve the patient and to eliminate the virus is to destroy, by the use of strong tincture of iodine or abiotic light, the epithelial cells which the virus has invaded. Sometimes it is necessary to extend the treatment to the whole surface of the cornea. Some broad-spectrum antibiotic should be used to combat secondary infection and later cortisone may be given for continued discomfort. Repeated vaccinations and a course of radiotherapy which consisted of four applications of 400r X rays or 400 r.e.p. beta rays at intervals of one week were used.

Disciform keratitis, a complication of dendritic or metaherpetic ulcers, responded to the use of cortisone and prolonged barbiturate sedations for the neuralgia. (5 references)

Lederman, M. **Radiotherapy.** pp. 193-207.

Radiotherapy is of value in treatment of some inflammatory processes by 1. reducing the vascular engorgement and the congestion accompanying inflammation or aiding in the eradication of unwanted blood vessels, 2. relieving pain, and 3.

promoting healing by assisting the resolution of the inflammatory exudate, the epithelization of an ulcerated surface, and the organization and removal of granulation tissue. (13 figures, 2 tables, 7 references)

Dudgeon, J. A. **Virologic aspects.** pp. 209-225.

The formation of antibodies in primary herpetic infection is extremely variable. Many persons harbor the virus and are subject to recurrent herpes by reactivation of the virus. The initial infection may remain strictly localized or spread in the form of vesicular eruption with a systemic reaction in the form of fever and adenopathy. Lesions in secondary herpes are invariably localized. Laboratory diagnosis of herpes simplex may be aided by such serologic tests as the neutralization or compliment fixation test. An increase in antibody can usually be detected in primary infections. In recurrent infection it is seldom possible to detect significant changes in antibody titer. It now seems certain that as far as the primary infection is concerned herpes follows the general pattern of an infectious disease. (5 figures, 25 references)

Beulah Cushman.

Gorman, J. J., Cogan, D. G. and Gellis, S. S. **An apparatus for grading the visual acuity of infants on the basis of opticokinetic nystagmus.** Pediatrics **19**:1088-1092, June, 1957.

Since the traditional opticokinetic drum appeared to be unreliable with infants, a simple but effective semicylinder of stripes on a roll of paper was devised. These stripes could be passed before the infants' eyes at a constant distance and controlled speed.

One hundred children were studied, varying in age from 80 minutes to five days; 93 responded to a 0.15 cm. wide stripe. This was calculated to be approximately equal to 20/670 visual acuity, allowance being made for motion. Acuity may have been better than this, but the method was not considered capable of greater accuracy. The test can at least be considered to give definite proof of the presence of vision. (1 figure, 1 table, 8 references) Harry Horwich.

Grossmann, E. E. and Thornfeldt, P. R. **Red glass X-ray spectacles.** A.M.A. Arch. Ophth. **58**:465-467, Sept., 1957.

The Corning Red glass is recommended as a lens for rapid dark adaptation for radiologists and others doing dark-room studies. (4 figures) G. S. Tyner.

Ham, O. **Acrylic ocular implants.** Arch. Chil. de oftal. **14**:35-41, Jan.-June, 1957.

The author gives a brief summary of the type of materials used for ocular implants and describes some of the ocular implants used during the last few years. He himself has used the Arruga type of implant with and without the two protruding tongues. He has had to remove a few implants, especially implants with protruding tongues, but he feels that good hygiene of the socket after surgery will eliminate this risk. The cosmetic result obtained with this type of implant is encouraging. (1 figure, 34 references)

Walter Mayer.

Hartmann, Karl. **Peritomy in various ocular diseases for the prevention of corneal complications.** Klin. Monatsbl. f. Augenh. **131**:526-530, 1957.

In this operation the bulbar conjunctiva is dissected from the limbus and mobilized. It was first devised by Passow for the treatment of chemical burns and can also be used in trachomatous pannus, recurrent corneal erosions and gonorrheal conjunctivitis. (33 references)

Frederick C. Blodi.

Heck, J. and Rendahl, I. **Components of the human electroretinogram.** Acta Physiol. Scandinav. **39**:167-175, 1957.

The photopic electroretinogram (ERG) in the light-adapted eye is carefully analysed as to form. Under the conditions employed by the authors, two negative and four positive waves are obtained. In normal eyes it is then demonstrated that adaptation to red light leads to disappearance of the third positive wave and that adaptation to green light leads to disappearance of the fourth positive wave. The variations of this phenomena which can be noted in the several subdivisions of color deficiency are then carefully described. A series of very interesting deviations results. In two totally color blind individuals, no photopic curve is elicited although a low normal scotopic ERG is obtained in the same eyes after dark adaptation. (3 figures, 26 references)

D. A. Mills.

Hogan, M. J. **Evaluation of vision screening methods in industry.** Arch. Indust. Health **16**:93-99, Aug., 1957.

This discussion is preceded by a glossary of visual terms for those not familiar with the science. The Snellen and Jaeger systems are then explained, and the efficiency of visual testing apparatus is discussed. It is observed that most of the visual screeners do not provide adequate charts for testing color perception. These devices are reliable for depth perception but skill is required for interpretation of these findings in relation to the actual individual situation. The same observation is made for muscle balance testing. The Harrington screener is found to be good for central fields, but a similar quick counterpart is needed for peripheral fields. Brief comments are made on corrective lenses for working distance, and on the problem of what constitutes the basis for referral of a screenee. Harry Horwich.

Hudelo, A., Hamery, A. and Perlmutter, B. **Ultrasound in ophthalmology.** Ann. d'ocul. **190**:684-697, Sept., 1957.

Ultrasonic vibration has been used in other fields to destroy tissue by its well known "cavitation" effect. The authors applied an ultrasonic generator in 33 cases of vitreous disease. Two frequencies were used: 960 kc and 1.2 megacycles. Of the 33 cases, 6 were considered hopeless before treatment and, as predicted, no improvement resulted. In the remaining 27 the authors felt there was some hope of amelioration of the vitreous disease process. These cases are analyzed from the point of view of etiology, type of ultrasound and interval between onset of disease and treatment.

The authors conclude that 1. the treatment is harmless, there is practically no pain associated with it and no patient was made worse, 2. the best results are obtained in eyes with free-floating masses in the vitreous, 3. one should allow three weeks for spontaneous healing before instituting therapy and 4. ten sessions of 8 to 9 minutes each are sufficient in most cases. (2 tables) David Shoch.

Imre, Gy. **Application of oxytetracycline in ophthalmology.** Szemeszet **1**:14-16, 1957.

Oxytetracycline, as a 0.5 percent solution or ointment, was applied in 150 patients. (The 0.1 percent ointment is inadequate.) The preparation proved efficacious in bacterial conjunctivitis, corneal ulcers, and epidemic keratoconjunctivitis. Corneal herpes proved resistant. Staphylococcus albus resistant to oxytetracycline occurred in three patients and resistant staphylococcus aureus in one. One patient was hypersensitive to the drug. Pseudomonas aeruginosa may cause conjunctivitis after operations or in infants. Oxytetracycline was effective in all cases, but the author found, on the basis of cultivation on various media, that 15 percent of the strains of pseudomonas aeruginosa occurring in his material were resistant to oxytetracycline. In corneal processes the cultivation of the agent and its ex-

amination for sensitivity should not be omitted. Gyula Lugossy.

Junceda Avello, J. and Roiz Noriega, M. **Refinements in our technique of roentgenography of the eyeball.** Arch. Soc. oftal. hispano-am. 17:1132-1135, Sept., 1957.

The authors had formerly published a description of a new method of localization of foreign bodies based on the perception of fine X rays by the retina, thereby localizing the posterior pole of the globe. The new refinements in the technique consist of better mobilization of the patient, by having him fix a rod between his teeth, and the utilization of the normal eye to find the posterior pole of both eyes, in cases in which the injured eye was so damaged that it could not perceive the localizing rays. At present the authors' efforts are directed to the development of a technique which will provide not only a linear identification of the posterior pole, but by multiple lines will outline also the posterior portion of the eyeball. (3 figures) Ray K. Daily.

Kapuscinski, Witold J. **The mechanism of fever therapy (typhoid vaccine) in eye diseases. (Introduction)** Klinika Oczna 27:231-232, 1957.

The author summarizes the results of work done under his supervision on the mechanism of fever therapy. His co-workers were able to demonstrate a shock phase after administration of typhoid vaccine before the antishock phase sets in, in accordance with the adaptation syndrome of Selye. Hormonal stimulation was also demonstrated by two other coworkers. The author deplores the fact that some physicians treat uveitis without removing the primary focus of infection. Sylvan Brandon.

Keller, B. **Anesthesia and pre-operative medication in ophthalmology.** Klin. Monatsbl. f. Augenh. 131:530-535, 1957.

The author presents a short outline of the routine medication given at the clinic in Frankfurt. The open ether drop method is apparently still in use for children and infants. Thorazine is advised before antiglaucoma operations. Vitamines B and C help to alleviate the discomfort after anesthesia. (2 tables) Frederick C. Blodi.

Kirsch, R. E., Samet, P., Kugel, V. and Axelrod, S. **Electrocardiographic changes during ocular surgery and their prevention by retrobulbar injection.** A.M.A. Arch. Ophth. 58:348-356, Sept., 1957.

The incidence of cardiac arrest has been estimated at one in 1,500 cases of general surgery, and one of 3,500 eye operations. The authors examined 50 eye patients during operation by serial electrocardiography and found significant changes in 30 percent. The stimuli which produced these changes were digital pressure on the globe, manipulation of extraocular muscles, and pressure in the orbital apex. A retrobulbar injection of an anesthetic always abolished these reactions and is, therefore, advised in surgery of strabismus, retinal detachment, or enucleation of the eyeball, either under local or general anesthesia. (6 figures, 22 references) G. S. Tyner.

Kornerup, Tore. **Visual and spectrophotometric examination of the eye with the slitlamp and monochromatic light.** Arch. f. Ophth. 159:323-342, 1957.

With monochromatic light one can examine the epibulbar and retinal vessels more effectively than with ordinary light. The possibilities of the Zeiss slitlamp can be extended through the use of variable monochromatic light. The best means of accomplishing this are described. A spectrophotometric method for determining relative oxygen saturation was developed which has prognostic value, particularly in penetrating injuries. (12 figures, 24 references) F. H. Haessler.

Kotania, Wladyslaw. **Shock phase in fever therapy stimulation.** Klinika Oczna **27**:239-245, 1957.

Clinical experiments on 25 patients were designed to show the shock phase after injection of typhoid vaccine. By comparison with controls there was lowering of blood pressure in the majority of patients which reached its maximum in eight to 15 minutes. Leukopenia appeared and was greatest after three minutes. Toxic granules and hypersegmentation of leukocytes could be seen. No changes were found in the pulse, respiration, body temperature and reflexes. Red cells and the quantitative morphology of the white cells were the same. The author feels that typhoid vaccine produces an abortive shock which is followed by the defense phase of bodily reaction. (2 figures, 4 references) Sylvan Brandon.

Krudysz, J. and Kleczenski, A. **Influence of fever therapy on excretion of neutral ketosteroids in urine.** Klinika Oczna **27**:247-354, 1957.

A short classification of the steroids found in the human organism precedes the description of the author's experiment. The behavior of neutral 17-ketosteroids was measured by Zimmerman's method. In 12 patients with uveitis the amount of 17-ketosteroids was checked before and after administration of typhoid vaccine. It was found that in 10 of them the elimination of steroids was lower than average. Injection of typhoid vaccine caused definite increase of elimination of neutral 17-ketosteroids in nine of 12 patients. This increase lasted for 48 hours. There was no relation between the cause of the disease and the level of steroids in the urine. (1 table, 3 references) Sylvan Brandon.

Laiseca Negro, Juan. **Artificial eyes.** Arch. Soc. oftal. hispano-am. **17**:1103-1111, Sept., 1957.

The merits and defects of prostheses made of glass, of an alloy of enamel and crystal, and of plastic are discussed. The author considers eyes made of an enamel crystal alloy as the most comfortable, tolerable, and coming closer in simulating a real eye. He emphasizes the importance of having the prosthesis fill the orbit without pressure. Free spaces between the artificial eye and the conjunctival sac lead to a proliferation of connective tissue and shrinking of the orbital cavity. He also describes a plastic plate which is used as an intermediate piece between the Arruga implant and the prosthesis; it eliminates irritation of the lids by the pins, when the prosthesis is removed, and simplifies the changing of the prosthesis. (4 figures). Ray K. Daily.

Long, J. C. and Tyner, G. S. **Three cases of epithelial invasion of the anterior chamber treated surgically.** A.M.A. Arch. Ophth. **58**:396-400, Sept., 1957

Three cases in which Maumenee's technique of treatment was used are reported. In one case an excellent result was achieved, in one there was a functional failure and in one sympathetic ophthalmia developed, necessitating enucleation. Surgical removal is probably indicated in early cases, in view of the seriousness of the complication. (5 figures and 7 references) G. S. Tyner.

Macfarlane, W. V. **Progressive blindness due to posterior uveitis following antisyphilitic treatment for interstitial keratitis.** Brit. J. Vener. Dis. **33**:165-168, Sept., 1957.

The author warns that it is not universally recognized that local cortisone therapy may produce complete remission of signs of inflammation in the anterior segment of the eye while at the same time an acutely progressive destructive lesion may be invading the posterior segment. (6 references) Irwin E. Gaynon.

Meyer-Schwickerath, G. and Bohnen, K. **Projection campimetry with polarized light.** Klin. Monatsbl. f. Augenh. **131**:363-367, 1957.

The patient wears polaroid spectacles and the target is visible to one eye only. Both eyes see the markings on the tangent screen which is projected independently to ensure binocular fixation. The target is projected as a dot and ocular central scotomas can be plotted quite easily. (3 figures, 4 references) Frederick C. Blodi.

Misar, Rainer. **The examination of the perifoveal field with the Goldmann perimeter.** Klin. Monatsbl. f. Augenh. **131**:367-375, 1957.

The attachment for plotting a central scotoma can be used for determining the perifoveal field. With the appropriate arrangement of the supplementary mirrors this important part of the field can be examined while the other eye fixates. Orthophoria must be present. (30 figures, 4 references) Frederick C. Blodi.

Mosquera, M. and Accame, E. A. **Toxic amblyopia due to 6-mercaptopurine.** Arch. oftal. Buenos Aires **32**:215-220, Aug., 1957.

In two cases of myeloid leukemia, one acute in a 13-year-old girl and one chronic in a 27-year-old woman, visual disturbances in the form of complete blindness or in that of wedge-shaped central scotomata appeared after the ingestion of 6-mercaptopurine in the usual doses for three and a half month and two years, respectively. Complete recovery occurred in a few weeks after the drug was withdrawn. In one patient, treatment could be resumed afterward without untoward consequences. (2 graphs, 3 charts, 13 references) A. Urrets-Zavalia, Jr.

Musial, Albin. **Results of treatment with mustard nitrogen in 150 cases over a period of two and one-half years.** Klinika Oczna **27**:269-274, 1957.

The results of treatment with nitrogen mustard in 150 patients with various ocular lesions are described. A series of five injections of 1 to 2 mgs. was used. They were beneficial in inflammatory conditions, reducing pain and shortening the duration, of questionable benefit in atrophic conditions of the optic nerve, and of no help in macular degeneration and retinitis pigmentosa. (9 references)

Sylvan Brandon.

Nagai, S. **Blister plaster test in allergic eye conditions.** Acta Soc. Ophth. Japan **61**:1725-1749, Sept., 1957.

In patients with such allergic conditions of the eye as vernal conjunctivitis, phlyctenule, irido-cyclitis, and central serous chorioretinitis, the blister appeared in a short time after the application of a blister plaster. The pH of the blistering fluid was high, and the number of cells in the fluid was great. (16 tables, 19 references) Yukihiko Mitsui.

Németh, L. **Histamine test on the conjunctiva in focal diseases of the eye.** Szemeszet **1**:17-22, 1957.

Remky's conjunctival histamine test in eye diseases of focal origin is discussed. The Hungarian preparation Peremin, in dilutions from 1:10,000 to 1:500,000, was applied to 50 patients with eye diseases attributable to foci. Fifty patients whose eye disease had nothing to do with foci served as controls. The author discusses the characteristic signs of positive response. The results of the histamine test and those of clinical investigation for foci agree well. The agreement was particularly striking in the histamine-positive cases of the first group exhibiting, on clinical examination, signs pointing to a focus in 80.7 percent. A strongly positive histamine test is a sign of focal infection; general examination is, however, not superfluous. The results show that other foci than those on the head, and remote foci, for example those situated in the lungs, may also give rise to a positive response. By performing the test on both eyes no information should be expected in regard

of the site of the focus. A positive test associated with equivocal results in the clinical examination speaks for an active focus and suggests the decision to eliminate it. On the other hand, a negative test associated with the clinical suspicion of a focus is a contraindication against surgery. The test is, if properly evaluated, a useful help in ophthalmology.

Gyula Lugossy.

Palomar Collado, F. **Palomar Collado's universal optotypes with two or more points of reference. Adaptation of this method to measuring visual acuity in hundredths or thousandths.** Arch. Soc. oftal. hispano-am. **17**:494-504, May, 1957.

The author has been working for years to improve the precision of visual acuity tests in order to obtain precise data in industrial visual loss, and in following the course of visual acuity in ophthalmoneurologic and neurosurgical cases. In 1942 the author described universal optotypes, constructed scientifically, with the minimum visible calculated for each distance. In 1951 he presented optotypes graduated in hundredths of visual acuity. In 1952 he added to the optotypes multiple points of reference. In the present chart the optotypes are constructed to measure visual acuity also in thousandths, for people with very low visual acuity. The author believes that the new chart permits of greater precision in the determination of visual acuity in examinations for professional aptitudes, in the determination of the extent of recovery from amblyopia, and for ophthalmoneurologic pre- and postoperative examinations. A chart is presented on the ordinate of which is the visual acuity and on the abscissa the distance at which the visual acuity is taken. The horizontal lines on the chart have a double scale showing the visual efficiency and visual loss in percentages. (3 figures, 8 references) Ray K. Daily.

Primrose, J. **Maddox rod as a test of retinal function.** Tr. Ophth. Soc. U. Kingdom **76**:323-327, 1956.

The author used the Maddox rod as a test of the condition of the fundus in patients whose cataracts were dense. Holding the red Maddox rod horizontally or vertically in front of the patient's eye in a dark room he asks for the color and the patient usually reports a line often with some beading; then he asks the patient to look at the center of the line and tell whether it is straight or wrinkled, whether it is of even thickness or thicker or thinner in the center. The test incorporates the color test; the center part of the streak tests the macular function, and the ends test the projection. The patients comprehended the test quickly. (7 references)

Beulah Cushman.

Radnot, M. **Application of hydergin in ophthalmology.** Szemeszet **1**:7-9. 1957.

Preoperative withdrawal of blood is not a proper measure to prevent bleeding. Adequate reduction of blood pressure can be frequently brought about by hydergin administration. The effect of hydergin should be tried before operation.

Gyula Lugossy.

Řehák, S., Bartoušek, V. and Dubanský, B. **Cobaltchlorophyllin (erythrophyll) in several diseases of the eye.** Arch. f. Ophth. **159**:347-350, 1957.

In a preliminary report the authors describe their experience in the use of erythrophyll in trophic disturbances of the cornea and in inflammatory diseases of the optic nerve. The results were encouraging. (2 tables, 6 references)

F. H. Haessler.

Rintelen, F. and Hotz, G. **The prophylaxis of blennorrhea of the newborn. Desogen as a new prophylactic.** Schweiz. med. Wchschr. **87**:1198-1201, Sept. 21, 1957.

The methods of prophylaxis used in 34 obstetric clinics in Europe are discussed. One percent silver nitrate is still considered to be very effective. No allergies or bacterial resistance have been noted, although 30 percent of the cases show conjunctival irritation. The sulfonamides and penicillin are no longer used.

A one-half percent solution of Desogen (Geigy) dyed with methylene blue is recommended on the basis of bacterial and clinical investigations. The effect on virus infections, sensitivity, and the problem of resistance remains to be worked out. (8 references) Irwin E. Gaynon.

Rodriguez, L. and Ferrari, J. **Potentialization of anesthesia.** Arch. chil. de oftal. 14:29-34, Jan.-June, 1957.

The authors emphasize the advantages of potentialization in ocular anesthesia; it reduces the total amount of anesthetic to be used, and it brings about total relaxation of the patient and with a complete postoperative amnesia. They describe their method of premedicating the patient the night before surgery with Largactil, a ganglioplegic of the entire nervous system, and Phenergan. This same combination is repeated in the morning of the operation, and about one and a half hour before the surgery the patient is given an infusion of Largactil, Phenergan, Demerol and saline solution, in variable amount, depending on the weight of the patient. This is followed by retrobulbar and subconjunctival injection of procaine and adrenaline and anesthesia with tubocurare.

The authors feel that this method of anesthesia makes possible much intraocular surgery, without danger of vitreous loss as a result of ocular hypotony. (3 tables) Walter Mayer.

Ruiz Rivas, M. **Functional radiotherapy in ophthalmology.** Arch. Soc. oftal. hispano-am. 17:1136-1145, Sept., 1957.

A radiologist defines the sphere of usefulness of X-ray therapy in ocular diseases other than neoplasms and gives the details of irradiation technique for each disease. He points out that for successful therapy close cooperation between the ophthalmologist and radiologist is essential and invites the cooperation of ophthalmologists in the treatment of vitreous hemorrhages, grave and resistant cases of iritis and iridocyclitis, grave cases of corneal dystrophy, imminent vascularization of corneal grafts, and thrombosis of retinal veins. Ray K. Daily.

Salgado Comez, Fernando. **The therapeutic value of sodium propionate in ophthalmology.** Arch. Soc. oftal. hispano-am. 17:1146-1164, Sept., 1957.

The author reports an experimental study on rabbits, and a clinical analysis of 141 cases, as to the effectiveness of sodium propionate in diseases of the anterior portion of the eyeball. The data which are reported statistically and graphically do not confirm Wellton and Charlotte's or Theodore's claims on the effectiveness of this therapeutic agent. Its chief merit appears to be its tolerability. It causes no irritation or allergic manifestations on prolonged application and therefore can be prescribed to hypersensitive patients. It is useful in acute bacterial conjunctivitis as an adjunt to more powerful therapeutic agents. After the acute stage has passed, its use alone will lead to recovery. In Morax-Axenfeld conjunctivitis its action is slower than that of zinc sulphate. It is ineffective in epidemic and follicular conjunctivitis, in spring catarrh and allergic conjunctivitis and blepharitis, in dendritic, nummular and disciform keratitis, and Mooren's ulcer. Its action is inconstant in chronic conjunctivitis, but is very good in seborrheic blepharitis. In ulcerative blepharitis it is an effective adjunct to other therapy. It is effective, although inconstantly so, in catarral corneal ulcers. It

is useful prophylactically in corneal erosions. (7 graphs, 3 tables)
Ray K. Daily.

Straub, W. **The influence of ethyl alcohol on the human electroretinogram.** Arch. f. Ophth. **159**:353-358, 1957.

Electroretinograms were taken on four men during the course of ingestion of alcohol. After the alcohol level had risen, no change in the latency, peak and duration of the b wave was demonstrable. However, there were individual differences in the increase in amplitude of the b wave although this change was not proportionate to the level of alcohol concentration in the blood. The maximal height of the b wave occurred with an alcohol level between 0.5 and 0.7 pro mille which was most obvious with low intensities of stimulation (1 to 7 lux). If the blood alcohol level rose above these levels the b-potentials became flatter. (4 figures, 13 references) F. H. Haessler.

Trichtel, F. **A new instrument for iontophoresis in iodine therapy.** Arch. f. Ophth. **159**:391-395, 1957.

The author describes an instrument which makes any desirable combination of thermic and iontophoretic effect possible. It is easy to manage and is reliable. (1 figure, 24 references) F. H. Haessler.

Trichtel, F. and Schenk, H. **Experiments with radioiodide for iontophoresis.** Arch. f. Ophth. **159**:343-346, 1957.

The radioiodide content of the aqueous was determined in the eyes of man and animals after iontophoresis with labeled iodine (I^{132}). In animals 30 to 78 times the concentration of iodine entered the anterior chamber during iontophoresis done with the eye open than when the lids were closed. In two patients no appreciable increase in concentration of iodine occurred in the aqueous after iontophoresis through closed lids. (2 tables, 14 references) F. H. Haessler.

Vannini, Angelo. **Normal and pathological gonioscopic pictures.** Rassegna ital. d'ottal. **26**:161-165, May-June, 1957.

The differentiation of the numerous processes which one observes in the iris of certain normal eyes with markedly developed trabeculae, in healthy eyes with monolateral hydrophthalmos, and in eyes with some abnormalities of the anterior segment is difficult. In high hyperopia the changes in the trabeculae may be similar to those observed in congenital malformations. The region of the angle in the zone of transition between the iris root and the ciliary body in the normal eye may assume a pathologic appearance in gonioscopic examination. (11 references)
Eugene M. Blake.

Weihmann, M. **Enucleation without excessive hemorrhage.** Arch. f. Ophth. **159**: 351-352, 1957.

The author describes a modification of the American neurotome which consists of a clamp in the form of the well-known enucleation scissors into one arm of which a sickle of spring steel has been incorporated. After the nerve is clamped one can withdraw the sickle (really a slender hook with a knife-like concavity) with two fingers and sever the optic nerve. (3 figures) F. H. Haessler.

Wiegand, H. R. **The anatomic and technical principles for obtaining simultaneous X-ray pictures of both optic canals.** Klin. Monatsbl. f. Augenh. **131**: 452-487, 1957.

The author first repeated some of the anatomic studies of Goalwin. Casts were made of the canals and it was found that the internal opening is a horizontal oval and the orbital end a vertical oval. The plane of the orbital opening subtends an angle of 22 degrees with the horizontal.

Technique: The head lies with the zygoma and the external orbital rim on the table. The horizontal subtends with the long axis of the table an open angle of 75 degrees. The sagittal suture line subtends an angle of 45 degrees with the plane of the table. The skin-target distance is 100 cm. The target is a point 2.5 to 3 cm. behind the external auditory canal and 1 to 3 cm. above the horizontal. This detailed paper should be of interest to many radiologists and ophthalmologists. (19 figures, 3 tables, 86 references)

Frederick C. Blodi.

6

OCULAR MOTILITY

Borishpoletz, V. **Surgical-orthoptic treatment of concomitant convergent strabismus.** Vestnik oftal. 5:37-45, Sept.-Oct., 1957.

The author emphasizes two stages in the treatment of concomitant strabismus: 1. correction of the anomaly of refraction and elimination of other hindrances to binocular vision, and 2. restoration of normal binocular coordination by orthoptic exercises. During the first year of life alternating occlusion is used, from the age of one to three years corrective glasses should be worn with occlusion of the fixating eye and after three years Bengerter's pleoptic method should be applied. Surgery should be done at the age of six or seven years. Orthoptic training combined with surgery resulted in complete cosmetic and functional cure in 12 of 25 patients with convergent strabismus. In the others the result was less good because of various factors: a vertical component, weakening of convergence because of a previously performed tenotomy of the medial rectus, and inadequate orthoptic exercises. Olga Sitchevska.

Ehrich, Wulf. **The latest squint therapy.** Med. Klin. 52:1634-1636, Sept. 13, 1957.

Wulf gives a classification of squint but feels that in the majority of the cases a combination of different components is present. Convergence insufficiency is present in almost every case, and the accommodation-convergence ratio is disturbed in most of the cases. If the squint amblyopia should be treated, then pleoptic therapy is undertaken and if the binocular vision is disturbed with good visual acuity in each eye, then orthoptic therapy is advised. All the clinics that are giving these treatments are under the supervision of an ophthalmologist. It is important to make an accurate diagnosis of the affected muscles and to give orthoptic therapy before and after surgery. To avoid scar formation of the muscle tissues, exercises are given on the muscle trainer after surgery. No definite conclusions have been reached on the medical treatment with bellargal and the eyedrops of mintacol. The results of the orthoptic treatments are not too favorable, but even little improvement is appreciated by the patients. Stephen G. Seech.

Fois, A. and Frezzotti, R. **EEG findings in concomitant strabismus and other ocular diseases.** Acta Paediat. 46:431-437, Sept., 1957.

The authors have detected a high incidence (approximately 50 percent of EEG abnormalities in patients with concomitant strabismus. The patterns noted include both diffuse and focal abnormalities. Abnormal records were seen in equal frequency in patients with alternating and unilateral strabismus as well as in patients with and without amblyopia. They compare this high incidence with a 10-percent incidence in the normal population and speculate about the role of the central nervous symptom in the pathogenesis of the oculomotor abnormalities.

David A. Rosen.

Galvez Montes, J. **Internuclear paralysis of the vertical conjugate movements.**

Arch. Soc. oftal. hispano-am. **17**:484-493, May, 1957.

The author reports a case of paralysis of elevation and paresis of depression in the right eye of a boy, five years old. The lesion followed a fall with injury to the skull and loss of consciousness. The optokinetic nystagmus was normal and of equal amplitude in both eyes. The movement of the affected eye was doubtful. The topographic diagnosis is discussed and it is concluded that a hemorrhagic lesion lies unilaterally between the centers of elevation and depression and the oculomotor nucleus. The literature on the diagnosis of such lesions is reviewed. (10 figures, 11 references) Ray K. Daily.

Gonzalez, F. **Correspondence in milimeters and degrees in cases of resection and recession operations on horizontal recti.** Arch. chil. de oftal. **14**:22-23, Jan.-June, 1957.

The author tabulates the correspondence between millimeters of resection of the horizontal rectus muscle and the degree of correction obtained in 21 patients operated upon by him for strabismus. (2 tables) Walter Mayer.

Piper, H. F. **The unstable relationships of the squinting eye to its environment and its significance as an immature asymmetry of the visual sense.** Klin. Monatsbl. f. Augenh. **131**:513-522, 1957.

The eyes of squinting children show an immature behavior which may be the result of an asymmetrical relationship to the environment. (3 figures, 17 references) Frederick C. Blodi.

Sternberg, A. and Molnar, K. **"Chinortho" eye drops in the treatment in certain cases of convergent strabismus and asthenopia.** Szemeszet **1**:9-13, 1957.

In the opinion of the authors, "chinortho" eye drops are frequently useful in accommodative esotropia and, within this group, especially in intermittent cases. Apparently, the success of therapy depends on the tendency to binocular vision. As there is no method of examination to predict whether or not this tendency is present, the authors suggest the application of the drug in all cases of accommodative convergent strabismus, all the more since this therapy is free of risk in youth. As a special treatment it may be suggested for asthenopia produced by accommodative esophoria.

Sixty years have passed since Javal expressed the view that the cure of strabismus is more than a series of cosmetic operations, and outlined the basic principles of orthoptic treatment, yet appropriate conservative procedures are still being sought for. Strabismus is a widespread disease and its therapy cannot be confined to a few orthoptic institutions. Practitioners need simple and efficient procedures leading to binocular vision. One of these procedures is "chinortho," at any rate in selected cases.

Gyula Lugossy.

Verzella, Mario. **Anesthetic block of the sphenoidal fissure.** Rassegna ital. d'ottal. **26**:226-230, May-June, 1957.

Infiltration of a local anesthetic injected into the orbital cavity acts well in recession operations but makes less exact the results in resections. The technique of the sphenoidal fissure injection is described and its value in 700 cases of strabismus convince the author of the great value of this procedure. If the technique is followed carefully, the procedure is without danger. (2 figures) Eugene M. Blake.

7

CONJUNCTIVA, CORNEA, SCLERA

Aberastain, Tomas G. **Lamellar, corneoscleral graft in marginal corneal dystrophy (Terrien's disease).** Arch. oftal. Buenos Aires **32**:195-197, July, 1957.

In a 43-year-old man whose right eye had been enucleated and who presented in

the remaining left one a marginal dystrophy of the cornea, rupture of this much-thinned membrane at the upper limbus seemed imminent. A lamellar, corneoscleral round graft, 10 mm. in diameter, was performed which encompassed the whole bulging area; at the latter's level only the epithelium was scratched, while a thin stromal layer was dissected away from the surrounding healthy cornea and sclera. The anterior chamber emptied itself partially through an accidentally produced small leak, in spite of which the operation could be completed successfully. Although, owing to the marked distortion of the anterior surface of the globe (which, as might be expected, remained unmodified), vision did not improve beyond the preoperative 0.1 reading, the result was excellent in that the graft kept its transparency, the demarcation gutter disappeared and with it every threat of rupture, the cornea being now of a uniform normal thickness. (3 figures)

A. Urrets-Zavalia, Jr.

Bennett, J. E. and Bailey, A. L. **Surgical treatment of total xerophthalmia.** A.M.A. Arch. Ophth. **58**:372-374, Sept., 1957.

The authors report their technique in successfully transplanting the parotid duct to the conjunctival sac in a case of total xerophthalmia in a 24-year-old male negro. (1 figure, 8 references)

G. S. Tyner.

Bennett, F. M., Law, B. B., Hamilton, W. and Macdonald, A. **Adenovirus eye infections in Aberdeen.** Lancet **2**:670-673, Oct. 5, 1957.

During 1956 there were 76 clinically diagnosed cases of viral conjunctivitis in Aberdeen; 37 patients developed nummular corneal opacities characteristic of epidemic keratoconjunctivitis. Five strains of type-8 adenovirus were isolated on human embryonic tissue culture from conjunctival scrapings. (2 tables, 9 references)

Irwin E. Gaynon.

Blatz, G. **Scleromalacia with rheumatism and mediasclerosis.** Klin. Monatsbl. f. Augenh. **131**:396-400, 1957.

In a 73-year-old woman with rheumatoid arthritis and scleromalacia perforans of the left eye, panophthalmitis followed the spontaneous perforation and an evisceration had to be done. The histologic examination showed the typical picture. Unusual was the marked mediasclerosis of the arteries of the lower extremities. (2 figures, 1 table)

Frederick C. Blodi.

Doggart, J. H. **Fuchs's epithelial dystrophy of the cornea.** Brit. J. Ophth. **41**:533-540, Sept., 1957.

This syndrome was first described by Fuchs in 1910 and except for the observations made by the slitlamp very little has had to be changed in the descriptions of its manifestations. It occurs in people in the sixth to seventh decade and affects women much more than men. Its etiology is unknown and there are no geographical, occupational or racial influences. The symptoms are progressive reduction in vision with haloes around lights. Examination reveals the bronze mosaic pattern of the endothelium with visicles of the endothelium, stroma and finally the epithelium. This progresses to large bullae and to destruction of the cornea with calcification. In the diagnosis, it is most frequently confused with early and progressive glaucoma and many patients with this disease have been subjected to glaucoma filtering operations. Treatment has been to no avail generally but the new surgical treatment of Paufique which consists of scraping the endothelium in the early stages by a curette introduced at the limbus, does promise some hope. (13 references)

Morris Kaplan.

Ferreira Filho, L. and Medina, H. **Primary cancer of the cornea. A contribution**

to its study. Arq. brasil. de oftal. **20**:22-32, 1957.

A 42-year-old man developed a rapidly-growing tumor in the pupillary zone of the right cornea two years after a corneal ulcer. The tumor was whitish in color with a pink tinge, 5 mm. square and occupied the entire pupillary area. The original plan of therapy was excision by means of a lamellar keratectomy, but enucleation was finally performed when it was seen that the tumor was more extensive than originally believed. Pathologic examination of the specimen confirmed the diagnosis of carcinoma, with the cornea as the point of origin. Final microscopic diagnosis was spinocellular (prickle cell) carcinoma of the cornea. The rarity of such tumors is emphasized. (5 figures, 25 references) James W. Brennan.

François, J. and Neetens, A. **Speckled hereditary dystrophy of the corneal stroma.** Acta Genet. Med. & Gemell. **6**:387-392, July, 1957.

The authors describe for the first time a type of hereditary corneal dystrophy which can be seen only with the slitlamp. Very small, clearly demarcated flat spots are visible in the stroma bilaterally. They are variable in shape and number, may be at any depth, and are not more numerous centrally than peripherally. The intervening tissue is normal and this dystrophy is not associated with any other condition, either ocular or systemic. Vision is not affected and the only symptom may be a slight photophobia. The mode of inheritance is that of a regular autosomal dominant and two pedigrees are illustrated. The condition is probably congenital since it is present at two or three years of age and does not progress during life. The authors differentiate this from Groenow's nodular dystrophy and from the cloudy hereditary corneal dystrophy which they recently described. (3 figures, 2 references) Edward U. Murphy.

Gáll, J. **The role of neurohormonal factors in the etiology of keratoconjunctivitis sicca.** Szemeszet **1**:38-42, 1957.

A change in the production of tears during the development of keratoconjunctivitis sicca, and the function of the gonads are interrelated pheomena. Its primary pathway is suggested to be neural, all the more since the lesion of the gonads is very soon followed by a drop in tear production. This correlation can be demonstrated in animal experiments also. The reduced value of the Schirmer test does not suffice to make a diagnosis of keratoconjunctivitis sicca. Several data support the view that diminished neural tonus is one of the factors playing a role in the development of the disease.

Gyula Lugossy.

Gimenez Almenara, Julian. **Dystrophic marginal corneal ectasia, or Terrien's disease.** Arch. Soc. oftal. hispano-am. **17**:456-461, May, 1957.

The literature is briefly reviewed, and a case which was under observation for six years is reported. A woman, 32 years old, gave a history of attacks of pain and recurrent attacks of irritation, which subsided spontaneously, in the left eye, for a period of four years. A marginal groove was found in the superior portion of the cornea close to the limbus. There the cornea was thinned at the expense of the parenchyma, and the grooved portion was anesthetic. It did not stain. Visual acuity was 1/8. The Wassermann reaction was positive and antiluetic therapy was prescribed. A guarded diagnosis of Terrien's disease was made. In the course of five years the patient developed a corneal ectasia with a marked increase in the irregular corneal astigmatism, and vision was reduced to 1/20. The development of the ectasia confirmed the authors early diagnosis. (2 figures, 5 references)

Ray K. Daily.

Kahán, A. and Vén, R. **Retroposition of the conjunctiva—a new approach to trachomatous entropion.** Brit. J. Ophth. **41**: 562-564, Sept., 1957.

Generally the effects of tarsectomy for entropion are unsatisfactory because of the retraction of the conjunctiva which produces lagophthalmos as well as blepharochalasis. In this modification of previous techniques the conjunctiva is lifted from the face of the tarsus and allowed to retract into the fornix. The uncovered area is then filled with a mucus membrane graft from the lip. The results have been satisfactory in 29 out of 30 cases. (5 figures, 1 table, 2 references)
Morris Kaplan.

Malhotra, Manmohan. **Plastic repair of conjunctiva with peritoneum transplantation.** Brit. J. Ophth. **41**:616-621, Oct., 1957.

Four cases are reported wherein transplanted peritoneum was used to repair the conjunctival sac with good results after about one year of observation. Peritoneum is easily obtained from many sources and can be stored in normal saline at 4 degrees C. for about 18 days. Very thin peritoneum is best obtained from hernial sacs and the tunica vaginalis from hydrocele sacs. In grafting one must be sure that the endothelial surface of the peritoneum is flush with the surrounding conjunctiva. Since peritoneum and conjunctiva are similar in color, thinness and transparancy, the cosmetic results are good. (8 figures) Lawrence L. Garner.

Marin-Amat, M. **Conjunctival hemorrhage and its treatment.** Arch. Soc. oftal. hispano-am. **17**:445-448, May, 1957.

The principal reason for this contribution is to describe the author's method of therapy. It consists of cauterization of the bleeding vessel or vessels with a fine platinum cautery point, after thorough anesthesia of the region with instillation of cocaine and adrenalin drops and application of cocaine crystals to the area to be cauterized. This procedure prevents the not unusual recurrence of hemorrhage from such vessels. The numerous causes of subconjunctival hemorrhage are discussed. (2 references) Ray K. Daily.

Mentz, E. **Bilateral keratoconus posticus circumscriptus.** Arq. brasil. de oftal. **20**:33-40, 1957.

Keratoconus posticus is a rare anomaly which has been observed in two forms: 1. general keratoconus posticus without corneal opacity which may occur more frequently than is ordinarily believed, and probably is a developmental defect; and 2. keratoconus posticus circumscriptus, in which the abnormal curvature of the posterior corneal surface is a central or paracentral excavation. The affected area shows opacification, and may be confused with a corneal leukoma. Several authors believe the cause to be an intrauterine infection or injury. Only nine cases have been reported, including the author's case. He describes a female patient who showed the corneal lesions in both eyes, a most rare phenomenon. In addition, a cataract was present in the left eye. The cornea showed a small, white, paracentral opacity in each eye. Visual acuity in the right eye was 1/10, not improved with correction. Refraction showed the presence of an irregular astigmatism. Slitlamp examination revealed the corneal changes, confirming the diagnosis. The anterior corneal surface appeared to have a normal configuration, while the zone of opacification showed thinning of the cornea, change of curvature and excavation in the location of the opacity. (2 figures, 7 references) James W. Brennan.

Meunier, A. and Zanen. **Conjunctival aneurysms in diabetics.** Bull. Soc. belge d'opht. **115**:234-240, 1957.

Sixty diabetics were examined carefully with the slitlamp. Fusiform or saccular

aneurysms and transitional forms of this variety were seen in 35 percent of the patients. Real berry-shaped aneurysms were seen in nine cases (15 percent); seven of these patients had a retinopathy. Berry-shaped aneurysms were considered as being found more frequently in diabetics but not as being either specific or pathognomic for this disease. (7 figures, 7 references) Alice R. Deutsch.

Nano, H. and Pérez, H. **Therapeutic lamellar grafts in chronic corneal ulcers.** Arch. oftal. Buenos Aires **32**:221-226, Aug., 1957.

After a long digression designed to demonstrate that the use of the term *graft* is legitimate in the case of corneal transplants (where obviously it is) and in that of vitreous inclusions (where, at least to this abstractor's mind, it is not), three cases of chronic, post-traumatic corneal ulcers are reported in which, all other treatments having proved ineffectual, the performance of small, peripheral lamellar grafts, either round or crescent-shaped, resulted in complete cure (cf. Franceschetti, A., and Doret, M.: Hornhauttransplantation "a chaud." Klin Monatsbl. f. Augenh. 117:449-458, 1950). In one instance, a pure culture of Pseudomonas aeruginosa could be obtained from the lesion). (8 figures, 1 table)

A. Urrets-Zavalía, Jr.

Otto, J. and Hild, E. **The metastatic furunculiform episcleritis.** Klin. Monatsbl. f. Augenh. **131**:541-544, 1957.

The authors report the development of staphylococcus bacteremia in two patients who had abscesses in the episclera. One patient had multiple furuncles in the axilla, the other patient a purulent pyelitis. (2 figures, 9 references)

Frederick C. Blodi.

Paczesniak, Roman. **A case of Sjøgren's syndrome.** Kinika Oczna **27**:289-292, 1957.

A 44-year-old woman with Sjøgren's syndrome had keratoconjunctivits sicca, atrophic rhinopharyngitis sicca and chronic rheumatic polyarthritis. She was given hormonal and antibiotic general treatment, vitamins and calcium, and locally chloromycin ointment and placental extract in the form of drops and injections. After ten weeks of treatment she left the hospital considerably improved, to return in seven months with the same complaints. The author feels that Sjøgren's syndrome is the result of hormonal and metabolic factors with superimposed virus infection. (3 references)

Sylvan Brandon.

Pisano, Elisa. **Hyperplastic papilloma of the cornea in trachoma.** Rassegna ital. d'ottal. **26**:118-126, March-April, 1957.

An 83-year-old man had had trachoma since early childhood and three-quarters of the surface of the cornea was covered by a dense hyperplastic tissue. The appearance of the new-formed tissue was that of a plasmoma but histologic study showed it to be a hyperplastic papilloma. (7 figures, 13 references)

Eugene M. Blake.

Preobrajensky, P., Bielousov, A., Orkodashvili, L., Djavadian, N., Lisogubov, V. and Pokrovsky, A. **The clinical picture and treatment of perforating wounds of the cornea in radiation sickness of dogs.** Vestnik oftal. **3**:10-13, May-June, 1957.

This experimental work was undertaken for the study of the clinical course and the treatment of perforating wounds of the cornea in 45 adult dogs with radiation sickness. In all animals a large trapezoidal wound was made in the upper segment of the cornea. In 15 dogs the healing of the corneal wound was observed without subjecting the animals to irradiation. In the other 30 dogs acute irradiation sickness was caused by irradiation with gamma rays (300 r.) of radioactive

cobalt. The cornea was left untreated in 15 of the irradiated dogs and in the other 15 dogs the corneal wound was sutured three days after the injury. Intramuscular and subconjunctival injections of penicillin were given during eight days. Atropin and abucid were applied to the conjunctival sac.

The animals developed irradiation sickness of second and third degree. The leucocytes in some animals decreased greatly. Despite blood transfusions seven out of 15 animals died 12 to 25 days after the irradiation.

A hand slitlamp was used to study the course of healing of the corneal wound and in some animals the eyes were enucleated and studied histologically. The fundus was normal in all animals. There was no appreciable difference in the healing of the penetrating corneal wound in animals which had been irradiated and those which had not. Corneal sutures applied three days after the injury were effective in the healing of the wound.

Olga Sitchevska.

Rapaport, M., Mieres, A. and Picoli, H. R. **Rhinosporidiosis of the conjunctiva.** Arch. oftal. Buenos Aires **32**:198-204, July, 1957.

Rhinosporridium, a parasite originally found in large nasal polyps by Seeber in Argentina, has been held responsible for the occurrence of granulomatous lesions of the conjunctiva in some 20 cases. After describing in full detail the features and the biologic cycle of the fungus, the case of a 26-year-old man is presented where this organism could be isolated from an abnormal conjunctival outgrowth measuring some 6 by 4 mm. (12 figures, 23 references) A. Urrets-Zavalía, Jr.

Regules Molina, Eladio. **Conjunctivitis and foci of infection in the pharynx and paranasal sinuses.** Arch. Soc. oftal. hispano-am. **17**:618-624. June, 1957.

The author emphasizes the importance of allergy in the intractable cases of nonbacterial conjunctivitis, with little secretion, with a tendency to remissions and recurrence, and in which asthenopia and a vascular factor play a part. The most important etiologic factor is the allergic personality of the patient. The sensitizing focus is sometimes difficult to find but is frequently found in the nose or pharynx. In some cases the allergic conjunctivitis is primary, and in others it may be secondary to other allergic manifestations originating in the same focus, and is produced in the conjunctiva through endocrine and metabolic processes. For this reason treatment of the sensitizing focus and administration of an autogenous vaccine may be sufficient in many cases. Others are very resistant and require a thorough study of the patient by an internist. Three cases of this type of conjunctivitis are reported. In one the focus of infection was found in the tonsils, which were enucleated and an autogenous vaccine prepared from the tissue. The patient recovered under this treatment. The second patient recovered from the conjunctivitis and headache, and from irritation of the pharynx and larynx after immunization with an autogenous vaccine from the pharynx. The third patient recovered after maxillary sinus surgery. (1 figure, 8 references) Ray K. Daily.

Rodgers, F. C. **Some observations on the punctate keratides in Africa.** Brit. J. Ophth. **41**:599-612, Oct., 1957.

The various types of punctate keratitis are described as they are seen in Africa. Dendritic keratitis is relatively rare but punctate corneal opacities of a similar type are seen in trachoma, leprosy and onchocerciasis. The latter is the only one that simulates the epidemic virus keratoconjunctivitis. Skin and conjunctival biopsies and the anterior uveitis usually seen in onchocerciasis aid in the differential di-

agnosis. The histopathology and etiology of the isolated lesions are described. (4 figures, 23 references)

Lawrence L. Garner.

8

UVEA, SYMPATHETIC DISEASE, AQUEOUS

Bangerter, A. and Hohl, K. **Contribution to the differential diagnosis of choroidal tumors.** Schweiz. Med. Wchschr. **87**:1195-1198, Sept. 21, 1957.

A short discussion of the differential diagnosis of tumors of the choroid precedes a description of the authors' method of X-ray irradiation for tumors in the posterior portion of the globe. The irradiation has a therapeutic effect on hemangioma and choroidal hemorrhage, it destroys tumor cells and prevents the outflow of lymph thereby diminishing the danger of metastasis following enucleation, and is also an aid in the differential diagnosis of intraocular tumors. (2 figures, 12 references)

Irwin E. Gaynon.

Bitran, D. and Pasmanik, S. **Congenital hyperplasia of the iris.** Arch. chil. de oftal **14**:56-57, Jan.-June, 1957.

The authors describe a patient with congenital bilateral hyperplasia of the iris, with an almost complete duplication of the iris. The supernumerary irises had plaques of atrophy and tears through which the underlying iris, which appeared to be normal, could be seen. The patient also had chronic simple glaucoma; the angle was completely open, and tension was well controlled with miotics.

Walter Mayer.

Kapuscinski, Witold J. **Clinical and experimental observations of the hyperergic and bacteriotoxic factor in uveitis. (Introduction)** Klinika Oczna **27**:209-214, 1957.

The author discusses recent ideas on focal infection and the pathogenesis of secondary foci. A neuro-vegetative mechanism is also mentioned. Two kinds of allergic reactions are described, one, in the usual way of anaphylactic reaction to protein antigen, and the other one, of local character, caused by direct contact of tissue with bacteria. The first type of reaction is characterized by liberation of "H" bodies and differs considerably from the second type. The author's investigations of uveitis showed that the allergic reaction is not the most important factor, and that bacteria and their toxins play a very important part in the pathogenesis.

Sylvan Brandon.

Pacynska, Julia. **Frequency of uveitis in pulmonary tuberculosis.** Klinika Oczna **27**:259-261, 1957.

Among 500 patients with pulmonary tuberculosis 21 were found to have changes in the uveal tract. Three of these were of traumatic origin, in 16 patients the lesions were peripheral and fully healed and in only two patients were choroidal foci found which were central and preceded by a pulmony infection. Only the last two cases can be considered definitely tuberculous in origin. The author's findings are similar to those of American, Russian and Italian investigators but lower than those of Germans. (1 table)

Sylvan Brandon.

Rossi, Antonio. **Rubeosis iridis.** Rassegna ital. d'ottal. **26**:166-176, May-June, 1957.

The author points out that rubeosis iridis is generally attributed to diabetes mellitus but actually there are other causes of this condition. Morphologically, the pictures are almost identical. One form of the disease results from the glaucoma secondary to thrombosis of the central retinal vein and occurs only after increased intraocular pressure, and is actually the result of circulatory stasis.

The usual rubeosis precedes the increased ocular pressure. (28 references)
Eugene M. Blake.

Rossi, A. and Pettinati, S. **Roentgen therapy in inflammatory affections of the uvea.** Rassegna ital. d'ottal. **26**:201-213, May-June, 1957.

The authors conclude that the results which they have obtained by therapeutic doses of X rays in inflammatory processes of the uvea have been particularly brilliant and they recommend its application even in cases where only slight improvement has followed. The authors emphasize that no damage has been done to the membranes of the uvea by radiation, even in instances where the treatment had been administered some years earlier. (32 references) Eugene M. Blake.

Sobanski, J. and Zelawska, H. **Etiology of choroidal detachment after intraocular surgery.** Klinika Oczna **27**:285-288, 1957.

Detachment of the choroid was observed after cataract extractions in 14 of 294 patients, evenly divided between the intracapsular and the extracapsular extractions. It was found in seven patients after Elliot's trephining which was done in 146 cases. There was no choroidal detachment after 65 iridectomies and four Lagrange operations. Detachment appeared usually between the sixth and thirty-fourth day after surgery and became flat between the fourteenth and the forty-first day. The authors usually waited seven to nine days for spontaneous regression. In three cases posterior sclerotomy was performed to release subchoroidal fluid. In all cases reattachment was complete. The detachment is usually caused by rigidity of the sclera in the presence of considerable outflow of intraocular fluid through the surgical wound. Waiting nine or ten days for reattachment may cause partial or total angle closure. (5 references) Sylvan Brandon.

9

GLAUCOMA AND OCULAR TENSION

Diaz Dominguez, D. and Ruiz Barranco, F. **Causes of error and erroneous data in tonography.** Arch. Soc. oftal. hispano-am. **17**:589-601, June, 1957.

This is a detailed analysis of the factors involved in erroneous findings in tonography. The effect of anesthesia, emotion, defects in technique, scleral rigidity and the mathematical formula are discussed in detail. The finding of an abnormally low tension is due to an error in the calculating formula. Failure of tensional variation is due to peripheral synechia. A rise in tension instead of a fall, found in 6.7 percent of the authors' cases, is attributed to changes in the blood vessels and vitreous. (14 references) Ray K. Daily.

Higuchi, S. **Relationship between anthranilic acid metabolism and glaucoma surgery.** Acta Soc. Ophth. Japan **61**:1519-1525, Sept., 1957.

Anthranilic acid was introduced as an agent which counteracts glaucoma by Iinuma who believed that an abnormal metabolism of tryptophane may play a role in the manifestation of glaucoma. The present author studied the possible relationship betwen surgery for glaucoma and the anthranilic acid metabolism of the system. After iridectomy in rabbits there was a considerable increase in the excretion of anthranilic acid in the urine for nearly ten days. He believes, therefore, that the action of iridectomy in counteracting antiglaucoma is not only the result of facilitating the outflow of aqueous but of increasing anthranilic acid in the system. (12 figures, 1 table, 24 references)
Yukihiki Mitsui.

Hilton Rocha. **Tonography.** Arch. chil. de oftal. **14**:5-21, Jan.-June, 1957.

The author summarizes the mathematical background of tonography and presents tables of tonographic values in his

glaucomatous patients. (7 tables, 16 references) Walter Mayer.

Küchle, H. J. and Rohrschneider, W. **Electroshock and intraocular pressure. II.** Arch. f. Ophth. **159**:433-438, 1957.

In 90 experiments in 48 rabbits the authors found no explanation for the reduction of intraocular pressure that results from muscular spasm. Injection of lactic acid, adenosine and lacarnol did not give evidence that an increase in products of muscle play a part nor did the contention of Wolff and de Jongh that a specific tension-reducing substance develops during muscular spasm. (4 figures, 3 tables, 28 references) F. H. Haessler.

Ruiz Barranco, F. **The basis and techniques of tonography. Data in normal eyes.** Arch. Soc. oftal. hispano-am. **17**:602-617, June, 1957.

This is an explanation of the mechanism of tonography, and the publication in Spanish of the Friedenwald and Koenig tables. The author points out that the electronic tonometer is not essential for tonography, and the data of this study were obtained with the Schiøtz tonometer. 170 normal patients were subjected to this form of tonography and the data are grouped according to decades of age to demonstrate the effect of age on the resistance to and facility of outflow. The data show that the ocular tension rises from 12.4 mm. Hg in the first decade of life to 18.7 in the fifth decade. From then it descends to 13.46 in the seventh decade and 16.09 in the eighth. The fall during tonography ranges from 6.5 to 8.5 mm. Hg, the greatest fall taking place during the first decade of life. The resistance to outflow rises from the first to the fourth decade of life; from then the rise is less pronounced and inconstant. The facility of outflow is greatest in the second decade of life, fluctuating afterwards, without any definite tendency to increase or diminish. In eyes with an ocular tension below 12 mm. Hg the outflow appears to be zero; the author believes that in such cases the venous pressure of 9 mm. Hg, which is assumed in the calculations of resistance to outflow is actually below that and the formulas are not applicable. The increased resistance to outflow with age lends support to the view that simple glaucoma is an exageration of senile processes. In over 100 cases the authors prolonged the time for tonography to ten minutes, and found no practical advantage in this prolongation. (2 figures, 9 tables, 9 references) Ray K. Daily.

Salgado Gomez, E. **The electroencephalogram in glaucoma.** Arch. Soc. oftal. hispano-am. **17**:468-475, May, 1957.

This is a preliminary report of a study of the changes in the encephalogram in glaucoma. The article is devoted principally to a description of the normal encephalogram. Five encephalograms in five cases of glaucoma are described. Reference is made to Hartman's work in this field, who found evidence of functional disturbances of the central nervous system in the encephalogram of glaucoma patients, with predominance of these disturbances in the left hemisphere. The author describes the changes in six electroencephalograms of glaucoma patients. (7 figures) Ray K. Daily.

NEWS ITEMS

EDITED BY DONALD J. LYLE, M.D.
411 Oak Street, Cincinnati 19, Ohio

News items should reach the editor by the 10th of the month. For adequate publicity, notice of postgraduate courses and meetings should be received three months in advance.

DEATHS

Dr. Harold Rexford Miller, New York City, died December 9, 1957, aged 61 years.

ANNOUNCEMENTS

GLAUCOMA COURSE AT MASSACHUSETTS EYE AND EAR INFIRMARY

A one-week course in glaucoma will be given at the Massachusetts Eye and Ear Infirmary, under the direction of Dr. Paul A. Chandler, April 28 through May 3, 1958. Topics to be considered will be: Ocular hydrodynamics; gonioscopy, tonography, and perimetry; diagnosis, medical and surgical management. Surgical demonstrations will be held in the operating room. Patients will be available for demonstration and examination. Admission will be limited to 10 persons. Fee: $100.00.

Application may be made to:

Dr. E. B. Dunphy
Chief of Ophthalmology
Massachusetts Eye and Ear Infirmary
243 Charles Street
Boston 14, Massachusetts

WILMER MEETING

The Residents Association of the Wilmer Ophthalmological Institute of The Johns Hopkins Hospital and University will hold its 17th annual clinical meeting at the institute March 27th through 29th.

FELLOWSHIP ESTABLISHED

The New York University-Bellevue Medical Center, Department of Ophthalmology, announces the establishment of the Daniel B. Kirby Fellowship for Research in the Ophthalmic Basic Sciences.

It is expected that candidates will have already demonstrated competence in research and that they will continue to work on basic problems. The appointment will be for one year at a basic stipend of $7,000.00, subject to renewal for two additional years. Laboratory space and facilities will be provided. Application should be submitted before May 1, 1958, to:

The Dean
New York University-Bellevue Medical Center
550 First Avenue
New York 16, New York

STANFORD CONFERENCE

The ninth annual spring postgraduate conference in ophthalmology will be presented by the Division of Ophthalmology of the Stanford University School of Medicine, March 31st through April 4th. The faculty of the conference includes:

Dr. Dohrmann K. Pischel, Dr. Jerome W. Bettman, Dr. Max Fine, Dr. Arthur Jampolsky, Dr. Earle H. McBain, Dr. David L. Bassett, Dr. William E. Borley, Dr. E. Homer Brugge, Dr. Bayard H. Colyear, Dr. Ernest W. Denicke, Dr. Victor Fellows, Dr. William J. Ferguson, Dr. Milton Flocks, Dr. Rufus C. Goodwin, Dr. Avery M. Hicks, Dr. Maurice S. Salomon, Dr. Thomas C. Stevenson, Dr. Edward Tamler, and Dr. Frank C. Winter.

SOCIETIES

IRISH OPHTHALMOLOGICAL SOCIETY

The Irish Ophthalmological Society will hold its annual meeting in Dublin on May 1st, 2nd, and 3rd. The Montgomery Lecture will be given by Prof. A. Hagedoorn, Amsterdam, in Trinity College, Dublin, on Thursday, May 1st.

PUGET SOUND ACADEMY

At the annual president's meeting of the Puget Sound Academy of Ophthalmology and Otolaryngology, the following new officers were elected: President elect, Dr. Willard Goff; secretary-treasurer, Dr. James L. Hargiss; trustee, Dr. George Drumheller.

At the close of the meeting the retiring president, Dr. E. DeMar Anderson, presented the gavel to the incoming president, Dr. Edison G. Dorland. During the meeting Dr. Lester T. Jones, Portland, read two papers on the lacrimal apparatus, and five new members were presented with certificates of fellowship in the academy.

PERSONAL

Mrs. Alina Drake, Chicago, has been appointed executive secretary of the Illinois Society for the Prevention of Blindness, 203 North Wabash Avenue, Chicago. She succeeds Mrs. Ben H. Gray who retired recently after 12 years with the Illinois society and who is now serving as a volunteer.

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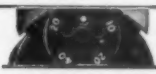

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The MODIFIED PANTOSCOPE illustrated is fitted with the "SELECT-A-LITE" switch-base which provides finger-tip brightness control as part of the 'scope. You can vary the illumination while observing the fundus. The "3-way & off" switch gives 6 volts for direct ophthalmoscopy in ordinary light, 9 volts for direct use in polarised light and 12 volts for all indirect ophthalmoscopy. It fits any Keeler 12v. 'scope.

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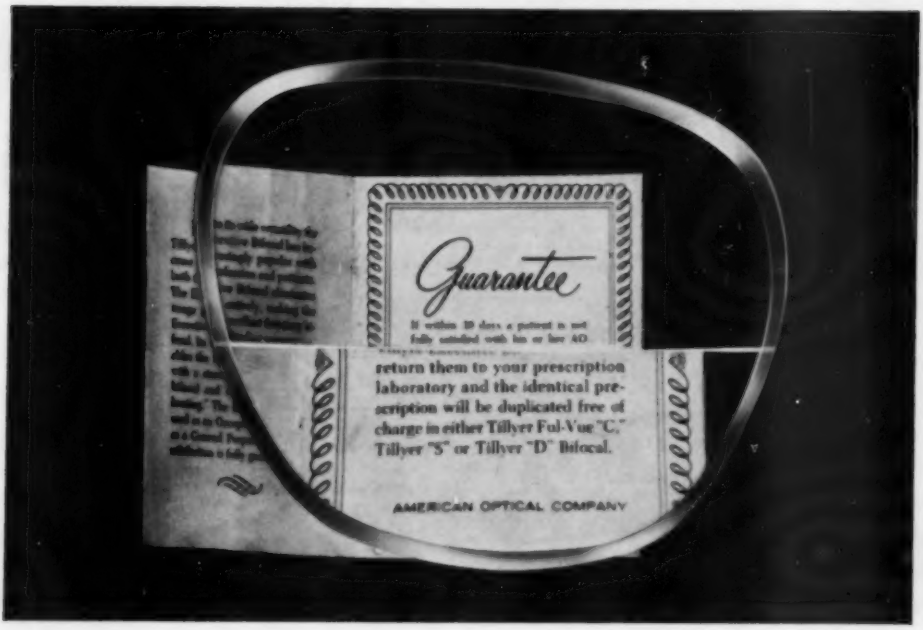

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4. THERE WILL BE ABSOLUTELY NO CHARGE TO YOU FOR THIS SUBSTITUTION.

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